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The Development of Brucellosis Control in Mongolia

Felix Roth

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Thesis submitted to the University of London
in partial fulfilment of the requirements for the Degree
Doctor in Public Health

London School of Hygiene and Tropical Medicine

Abstract

Previous economic analysis of brucellosis control in Mongolia provided a basis for further research. It was observed that there was a long tradition of brucellosis control in Mongolia but little knowledge on its effect on the spread of disease. This thesis addressed this gap and analysed the relationship between stated surveillance policy, the brucellosis prevalence in animals, and the brucellosis incidence in humans. The aim was to contribute to better understanding of the brucellosis surveillance policies applied in Mongolia and their effectiveness, and to draw conclusions and recommendations for control of brucellosis.

Four aims were formulated providing steps for investigating the research question. The first two aims focused on (i) the establishment of the epidemiological patterns of brucellosis in Mongolia over the time period 1966 to 2002, and on (ii) the provision of a historical overview of the different strategies applied to the control of brucellosis in Mongolia over the same time period. The third aim was to assess the interactions between the spread of brucellosis and the surveillance strategies, and finally the forth aim was to issue recommendations about future surveillance policies for brucellosis.

It was found that the published figures reflected the *Brucellosis abortus* incidence in the population that could be serologically tested. However, the population at risk (herders) with the main burden of disease, and suffering from *Brucellosis melitensis*, was underdiagnosed and not treated properly, additionally, the immunisation campaigns in small ruminants did not reach the critical vaccination level for eradication. Therefore, the diagnosis and treatment of *Brucellosis melitensis* in humans has to be assured at Soum (district) level. The current immunisation campaign has to be monitored and evaluated, and the knowledge of brucellosis in humans has to be recognised by policy makers, physicians and general population.

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DrPH Summary Statement

The Doctorate in Public Health (DrPH) is a professional doctorate and is target for those who expect their careers to be leaders in public health practice rather than research. Access to a wide range of skills and insights to various disciplines is needed to face the challenge of understanding and adapting scientific knowledge to achieve health gain. This is reflected by the programme for DrPH degree, consisting of three components:

- i) a taught component during the first 6 – 8 months of the programme, consisting of six units at least;
- ii) a professional attachment in an institution engaged in public health practice, giving the opportunity for reflecting on the practice of public health, and
- iii) a research project leading to the production of the thesis in hand.

Each of these components contributes to the award of the degree (*London School of Hygiene & Tropical Medicine, 2002*).

After 15 years of working experience as a health economist in different places and positions, I had wanted to underpin this practical professional experience with theoretical and current knowledge, and to broaden my approach with public health practice. The programme of DrPH means the ideal combination of scientific research and practical experience. Working first in public health insurance and committed to introducing managed care in Switzerland, I took over the managing lead of one of the first Health Maintenance Organisation (HMO) in Switzerland. Joining the Swiss Tropical Institute (STI) as senior officer in the directorate, I was managing various projects in Developing Countries. I followed up the DrPH programme part-time, working whilst as manager of the EQUAM Foundation (Zürich / Switzerland), promoting a quality label for quality management in primary health care.

During the teaching component (October 2001 to April 2002), I complemented the compulsory study units (*evidence-based Public Health Practice 1&2, Leadership and Management Development*) with introductory courses in epidemiology ("*Basic Statistics for Public Health and Policy*", "*Basic Epidemiology*" and "*Design & Analysis of Epidemiological Studies*"), and courses introducing research methods in social sciences ("*Principles of Social Research*" and "*Health Care Evaluation*") and a course on reviewing the literature. These courses equipped me well for conducting my research work: besides searching literature and assembling epidemiological figures, I collected and analysed qualitative data, and my epidemiology training helped me undertake the quantitative analysis.

The professional attachment was carried out at the Swiss Tropical Institute (STI), where I had broad insight. I developed, through the professional attachment, a deeper understanding of this organisation, observing and analysing the mechanism of how the STI contributes to public health and how this could be measured. The STI also provided the platform for (i) being the partner institution, together with the Mongolian Academy of Sciences, to establish the important research partnership to conduct my research work, and for (ii) publishing two papers on brucellosis control in Mongolia (attached in the pocket at the back).

My interest in brucellosis control in Mongolia arose from this previous work, where I was the coordinator of a research study on the impact of brucellosis on households, a survey with special consideration of its direct and indirect costs and on coping strategies. This allowed me to conduct the research work in one of the most fascinating areas, and address the problem of zoonosis control, a topic underestimated and challenging public health in developing countries worldwide. The difficulties of zoonoses control in nomadic settings have to be addressed with an interdisciplinary approach. This gave an opportunity to yield knowledge, skills and experience in such a working environment, uniting different methodologies and acknowledging an entire subject or problem. In this sense it contributed greatly to my becoming a Public Health professional.

List of Acronyms and Glossary

Aimag	Primary unit in Mongolia, i.e. province; it consists of several Soums
B	Brucellosis
Bag	Sub-district in Mongolia
CDC	Centers for Disease Control and Prevention (USA)
CFT	Complement Fixation Test
CGA	Central Governmental Archive
COMECON	Council for Mutual Economic Assistance
DrPH	Doctorate in Public Health
Dzud	Freezing snow or ice storm covering pasture
ELISA	Enzyme-Linked Immuno-Sorbent Assay
FAO	Food and Agriculture Organization of the United Nations
Feldsher	Rural health officer
Ger	Felt tent
GDP	Gross Domestic Product
HSDP	Health Sector Development Programme
IDRI	Infectious Disease Research Institute
IMF	International Monetary Fund
KFPE	The Swiss Commission for Research Partnership with Developing Countries
MAS	Mongolian Academy of Sciences
MBCP	Mongolian Brucellosis Control Programme
MoA	Ministry of Agriculture
MoF	Ministry of Finance
MoH	Ministry of Health
MPR	Mongolian People Republic
MRT	Milk Ring Test

O.I.E.	Office International des Epizooties; Organisation mon-diale de la santé animale (World Organisation for Animal Health)
ppp	purchasing power parity
RBT	Rose Bengal Test
RCHID	Research Centre of Human Infectious Diseases in Ulaan Baatar
RVC	Royal Veterinary College, London
SAT	Serological Agglutination Test
SIR-model	Susceptible Infectious Recovered model
Soum	Secondary unit in Mongolia, i.e. district, it consists of several Bags
SR	Small ruminants
SSOM	State Statistical Office of Mongolia
STI	Swiss Tropical Institute
TB	Tuberculosis
T&S	test and slaughter
UB	Ulaan Baatar
UN	United Nations
UNDP	United Nations Development Programme
USD	US-Dollar
USSR	Union of Soviet Socialist Republics
VPH	Veterinary Public Health
VRI	Veterinary Research Institute
WHO	World Health Organization (UN)
WS	Workshop
Y09	Yersinia enterocolitica 0:9

Introduction

The interest in the topic of the thesis arose from previous work on brucellosis control in Mongolia. Brucellosis control occurred for many years but remained unevaluated. The aim of the thesis was to analyse the possible interactions between the surveillance strategies applied to control brucellosis - and its spread - to formulate recommendations about future surveillance policies.

1. Brucellosis

Man and animals have long since lived with brucellosis. Hippocrates (450 bc) described brucellosis in humans (*Parnas J. et al, 1966*) and examinations of the skeletons of victims of the eruption of Mount Vesuvius (79 AD) reveal a high prevalence of brucellosis as bone lesions - typical of brucellosis - were found in 17.4% of the adults (*Capasso L, 1999*), presumably due to the consumption of milk from sheep and goats. During the 18th century this disease was commonly known in the Mediterranean region as “Malta fever”, “Mediterranean fever”, “Gibraltar fever”, “Crete fever”, “Neapolitan fever”, “Cyprus fever”, etc. The etiology of brucellosis was not known at that time. In the 20th century, brucellosis became recognised as a clinical entity. It was called “undulant fever”.

Brucellosis is a zoonosis caused by the bacteria from the *Brucella* group. *Brucella* species create chronic diseases persisting for life. In animals, the organisms is localised in the reproductive organs and cause abortion and sterility; these organisms are shed through the urine, milk or placental fluid. This facilitates infection not only to other animals but also to humans. *Brucella spp.* can survive for long periods outside the animal body and can enter the human body through food (un-pasteurised infected milk) or respiration, cutaneous contact, conjunctival contact. Transmission of

Brucella organisms from human to human is extremely rare. Human brucellosis is a febrile illness with varied clinical manifestations and may simulate other diseases. In the absence of specific treatment, human brucellosis may persist and progress to a chronically incapacitating disease with severe complications.

Despite the biotechnological improvements achieved during the last half century, brucellosis has remained one of the most important bacterial zoonosis worldwide (Young E, 1995) (Cutler S J et al, 2005) (Cutler S et al, 2003). Brucellosis was classified as a list B disease by O.I.E (Office International des Epizooties; Organisation mondiale de la santé animale), as being of importance from a socio-economic and / or public health points of view (see appendix 1.1 for list B). Only 17 countries were considered to be free of brucellosis (1994), and this status could only be maintained with a considerable surveillance investment (see appendix 1.2 for countries listed).

When present, this disease is a huge burden in developing countries, perpetuating poverty through the loss of productivity and livestock, and causes severe and debilitating disease in humans. Although controlled or even eradicated by rigorous surveillance policies in most developed countries, re-introduction of brucellosis remains a constant threat. WHO/FAO/O.I.E. joint consultation on emerging zoonotic diseases (WHO et al, 2004) considers brucellosis as one of the key zoonosis of concern, leading Dr. William Amanfu¹ to state: "This is the second most important zoonosis in the world after rabies" (Cutler S et al, 2003).

It is estimated that about half a million new human infections cases occur worldwide per year (Cutler S J et al, 2005) (Roberts A et al, 2001) (Araj G F, 1999) (Cutler S et al, 2003). This may not reflect the actual number, because brucellosis is not considered a notifiable disease in many parts of the world; there is no disease-reporting system in many countries, and relevant statistics are lacking or not comparable. Human brucellosis is considered to be under-diagnosed and under-reported (Madkour M., 2001). In developing countries, diagnosis is difficult, and reporting systems are

¹ Animal Health Officer (Bacterial and Zoonotic Diseases) at FAO/Rome

less reliable than in industrialised countries. But even in developed countries - where the disease is being controlled - a reporting rate of only 20% is estimated in France (*Foulon G et al, 1981*), and even less in Spain (8%) (*Aller B, 1975*), or the USA (3,5%) (*Wise R I, 1980*). More recent estimations report the ratio of reported to unreported cases of 1:26 (*Araj G F, 1999*), without giving more specific background information.

Despite the eradication in a few countries, brucellosis in humans and animals is increasing worldwide. Brucellosis was serious and longstanding in livestock and humans in the former USSR-Countries, such as Russia (Caucasus region) (*Flynn M P, 1983*) (*Liamkin G I et al, 1995*) and its central Asian states Kyrgyzstan (*UN Office for the Coordination of Humanitarian Affairs, 2003*) (*Kyrgyzstan Development Gateway Social sector annual data, 2001*), Tajikistan (*Jackson R et al, 2003*) and Kazakhstan. Despite the fact that these countries, with former centrally planned economies, had made considerable efforts to control brucellosis for many years, related data and published articles are very few (*Dobrean V et al, 2002*). The weakening of the veterinary system and the transition from large government controlled farms to small-scale private farming has lead to the re-emergence of brucellosis. The unequal distribution of the spread of brucellosis may reflect deteriorating control over the past 10 years, uncontrolled movements of livestock, and influences of environmental factors on local animal management practices (*Jackson R et al, 2003*). This situation fits the current situation in Mongolia, the focus of the thesis.

2. Mongolia

Mongolia has unique demographic and environmental characteristics which impact health significantly (*Government of Mongolia et al, 1999*). Few inhabitants (2.475 million) (*National Statistical Office of Mongolia, 2003*) who live in a large geographical territory of 1.566 million km² (*National Statistical Office of Mongolia, 2003*). Ensuring adequate health services throughout a sparsely populated terrain (only 1.58 inhabitant per km²) is a challenge. Providing access to health services for

rural populations who are semi-nomadic pastoralists is particularly difficult due to the long distances and poor road infrastructure compounded by the severe climatic conditions.

Mongolia had close political and economical relations with the Soviet Union from 1921 (Mongolian communist revolution) up to the collapse of the Soviet bloc 1989. The Soviet Union used to provide about a third of the Mongolian GDP (*WHO, 2005a*). This contributed to the gradual transformation of a society based on a nomadic lifestyle to a more industrialised and urban society.

The loss of former assistance, and trade from the Soviet Union, has led to severe economic difficulties. The GDP per capita dropped by about 20% between 1990 and 1993 (*World Bank, 1997b*). During the transition from a centrally planned economy to a market oriented economy Mongolia has seen dramatic changes in all aspects of the social, political and economic life. Since 1994, the GDP per capita has grown, with fluctuations, from per capita ppp-dollar 1290.-- in 1995 to 1710.-- in 2002² (*UN Common Database / World Bank, 2006*). However, there was a growing disparity between rural / urban and rich / poor. The fraction of GDP produced in the capital Ulaanbaatar (UB) had grown to 54.9% in 2001 (46.6% in 1999) (*National Statistical Office of Mongolia, 2003*). There is a high level of internal migration from rural to urban areas, leading to *ad hoc* urbanisation around urban centres particularly Ulaanbaatar. About a third of the population are poor (*United Nations economic and social council, 2002*), the fraction of poor in rural areas is increasing.

Traditionally, the survival of a major section of the population and of the country as a whole depended largely on breeding animals. “The main livelihood source and the wealth is livestock in Mongolia” (*National Statistical Office of Mongolia, 2003*). However, due to three consecutive harsh winters (2000 to 2002) the number of livestock has declined from 33.5 million in 1999 to 23.9 million in 2002, and the agriculture sector has experienced a sharp reduction; its contribution to GDP has declined from 38% in 1995 to 20.1% in 2002 (*National Statistical Office of Mongolia,*

² Ranking as 120th country in 2002 after Laos and before Bangladesh (as 134th country in 1995)

2003). As livestock production contributed to 78.9% of the total agriculture production, its contribution to GDP still reached 16% in 2002, and provided 5.5% of the national exports (*National Statistical Office of Mongolia, 2003*). The production is mainly nomadic and extensive.

The Soviet-style health system covered the entire nation, with universal access to hospital-based medical services provided free of charge. There was a strong preference for in-patient rather than ambulant care. The system was supported by community-based health workers (Bag Feldshers), Soum (district) health centres and Aimag (provincial) hospitals. The first Health Sector Development Programme (HSDP) (1997–2002) aimed at shifting the hospital based services towards a more responsive primary health care-orientated system based on family group practice (*WHO, 2005a*) (*O'Rourke M et al, 2001*). This has been implemented in urban areas. The second HSDP (2003-2008) focused on reforms to the first level of referral for rural health services, the Soum hospitals (*Hill P S et al, 2006*). The total health spending accounted to 6.2% of GDP (1998), representing per capita total health expenditure of USD 24, or expressed in ppp (purchasing power parity) of USD 88 (*WHO, 2005a*).

3. Brucellosis in Mongolia

Mongolia has a long history of brucellosis control, starting in the early 1960s with wide-scale epidemiological studies led by the WHO, and intervention programmes in animals assisted by COMECON States. After various control activities over decades, surveys conducted in the 1980s and 1990s among humans at risk, such as herders and workers in slaughterhouses, still confirmed high contamination rates: between 15% and 25% of the tested persons were sero-positive, and about 10% of the tested persons had active brucellosis (clinical signs). Brucellosis continues to be listed among the four major chronic infections, together with hepatitis B and C, tuberculosis and sexually transmitted diseases (STDs) (*Ebright J R et al, 2003*). Brucellosis is thus one of the major veterinary and public health problems. Important

in this context is the big population proportion being at risk: about 23%³ of the population live in rural areas and lead a nomadic or semi nomadic way of life (*Ebright J R et al, 2003*).

4. Previous work leading to the research question

Being a centrally planned country most livestock was the property of the State and kept in co-operative herds. This assured prescribed preventive measures taken by the herders. Along the transition in the early 1990s, introducing a market oriented economy, most livestock have been returned to private ownership and the state funding for animal health activities has been reduced and veterinary services privatised. To regain control of the increasing spread of brucellosis, the Mongolian Government adopted in 2000, on the recommendation of WHO, a whole-herd vaccination strategy, seen as the only feasible option and most appropriate approach.

Prior to the implementation of the whole herd immunisation, the economic implications and the effectiveness of this whole-herd vaccination programme was estimated by the author who on behalf of WHO and FAO conducted and coordinated a benefit-cost analysis and a cost-effectiveness analysis in 2000, with the technical support of experts from the RVC, WHO, FAO, STI, and in collaboration with Mongolian counterparts from the MoH and MoA (*Roth F. et al, 2001*).

The study concluded that mass vaccinations of livestock against brucellosis in Mongolia would be cost-effective and would result in net economic benefits, if the interventions costs were shared between the different beneficiaries on the basis of an intersectoral economic assessment.

In general, there are various factors on different levels which make control, eradication or prevention of brucellosis difficult. One set of hampering factors have eco-

³ Other source mention 28% (*Foggin, Peter M. et al, 1997*)

conomic, political and psychological origins: there were few studies, evaluating the costs of various methods to prevent, control, and eradicate this disease. An important impact of animal brucellosis is human disease and its associated costs. So it is both logical and necessary that both animal and human health authorities promote brucellosis control programmes and allocate their costs through an intersectoral approach. Only cost benefit analysis considering the overall costs and benefits for both the animal and human sectors can demonstrate their real benefits. Brucellosis often becomes chronic and fails to generate enthusiasm among livestock owners and others for longstanding control and eradication efforts.

The results of the study were therefore useful for policy-makers in determining strategies, and publication became an important issue. The topic has been split into two parts to better reach scientists. The first is oriented to health economics and health policy, whereas the second tackles dynamic modelling of transmission from animal to animal, and from animal to human. The paper estimating the economic benefit, cost-effectiveness and the distribution of benefit has been published in the WHO Bulletin (*Roth F. et al, 2003*). The other paper reporting the dynamic model of livestock to human transmission, which was developed as an underlying framework to estimate the profitability, has been published in the Preventive Veterinary Medicine (*Zinsstag J. et al, 2005a*). Both papers are enclosed in the pocket at the end of this thesis.

The involvement with policy and the analysis of the economic implications stimulated interest in previous policy to control brucellosis in Mongolia. It also provided a basis from which further research could be conducted.

5. Research question

The author observed that there was a long tradition of brucellosis control in Mongolia, but that unfortunately there was little knowledge of the effects these surveillance policies had had. Therefore, this thesis now proposes to explore these effects and provide a better guide to future control efforts in Mongolia. This crucial investigation has been greatly facilitated by the author's previous work on brucellosis control in Mongolia which established a data collection network in Mongolia, and important relationships with scientists, public authorities, policy makers, and health officers.

The central research question is to determine whether there was any relationship between the stated surveillance policy and the brucellosis prevalence in animals and humans between 1966 and 2002. To accomplish this aim the empirical evidence of epidemiological patterns in animals and humans had to be provided, as well as overview of the different surveillance strategies.

The observation period begins in the mid 1960s, the start of comprehensive surveillance activities and data collection. The elements of the applied surveillance policies have to be analysed to assess their possible effectiveness. The dataset on the epidemiological patterns allow quantitative analyses of the effects of surveillance policy on the spread of brucellosis. The findings allow addressing recommendations for brucellosis control policies in Mongolia.

6. Overview of the thesis

The characteristics of brucellosis are discussed in chapter 2., which provides an overview of the symptoms, transmission paths and techniques of diagnosis. The worldwide spread of brucellosis is analysed and the Mongolian situation put in this context. Basic elements of surveillance are elaborated and put in current context of

brucellosis surveillance, providing the critical elements for a qualitative policy analysis.

The research question is presented in chapter 3, and an overview given on the methodology applied for addressing it. This includes the definition of the type of information required, listing of the data sources, and describing the methodology for data collection during the field work in Mongolia, conducted in autumn 2003. The quality assurance of the collected data was an important aspect, as the data collection had to cope with the language barrier and constraints of conducting research in a large sparsely populated developing country. Its methodology is therefore described separately. Finally the methodologies leading to qualitative and quantitative analyses are presented.

The history and evolvement of brucellosis in Mongolia is elaborated in chapter 4, creating a comprehensive picture. The etiological aspects determining the sources, factors and routes of transmission gave important baseline information for assessing the surveillance policy.

The history of the different surveillance policies applied to the control of brucellosis in Mongolia is analysed in chapter 5. The policy papers provided detailed insight on the various elements defining the policies, and allowing further analyses carried out in chapter 6. Data collection on testing and vaccination allowed an assessment of the policy implementation with quantitative data.

Chapter 6 brings the spread of brucellosis (chapter 4) and the control policy (chapter 5) together by analysing possible interactions. Qualitative analysis of the surveillance policies opened the view on policy gaps and on further possibilities for quantitative analysis. The vaccination scheme was analysed with mathematical modelling, the animal human transmission with multiple regression. Both analysis, the qualitative and quantitative, allowed drawing conclusion on the applied policies and its effectiveness in controlling brucellosis.

The last chapter 7 summarises the main findings and discusses the limitation and contribution of the thesis. Recommendations for policy makers are formulated.

1. Characteristics of Brucellosis

History

In 1886, the British scientist David Bruce (who was later knighted) discovered on Malta micrococci probably causing the fever affecting British troops stationed in Malta. Microscopic examination of tissue from the spleen of soldiers dying after developing “Malta fever” (*Parnas J. et al, 1966*) had revealed them, and he called the organism *Micrococcus melitensis* after the Isle of Malta. In 1918, the bacteria would be named *Brucella* to honour this discovery. The infection’s reservoir in goats, however, was found only in 1905 by Sir Themistokles Zammit (*Parnas J. et al, 1966*).

The Danish veterinarian Bernhard L. F. Bang discovered in 1897 that the cause of cattle mass abortions in Denmark was located in infections caused by a bacteria he named “*Bacillus abortus bovis*”. Mass abortions in pigs also caused by bacterial infections were described in the USA in 1914 by Traum (*Madkour M., 2001*). Finally, in 1918, Alice Evans noticed the similarities between *micrococcus melitensis* causing “Malta Fever” in humans and the *Bacillus abortus* causing mass abortions in cattle, pigs, sheep and goats. *Micrococcus melitensis* was found to be a bacillus. The division of the pathology into human and animal, as well as insufficient collaboration between physicians and veterinarians all combined to delay the linkage between human and animal research.

In the late 30s, it was finally recognised that the fight against brucellosis in humans should begin with animals. After WW II, a WHO-Expert Committee on Brucellosis was created through the initiative of Martin Kaplan, head of the epidemiological department at WHO. The Office International des Epizooties; Organisation mondiale

de la santé animale (O.I.E.) became the coordination centre for collecting data on the Brucellosis reservoir worldwide.

The bacteria *Brucella*

Brucellosis is a zoonosis caused by the bacteria from the *Brucella* group. Genetically, it can be regarded as variants of a single species, with differentiation into six main species: *B. abortus*, *B. suis*, *B. melitensis*, *B. neatomae*, *B. ovis* and *B. canis*. This is of practical importance, as the epidemiology and the severity of the diseases in humans is influenced by the *Brucella* type and its source (Corbel M. et al, 2000): *B. abortus* is normally associated with cattle, *B. melitensis* with sheep and goats, *B. suis* with swine, *B. ovis* causes infections specific for sheep and has not been implicated in human diseases, *B. canis* is usually associated with diseases in dogs but occasionally causes human brucellosis, and *B. neatomae* has been isolated on few occasions and has never been implicated in human diseases. The most common *Brucella* species to affect humans is *B. melitensis*, the most pathogenic species producing the most intense symptoms, the greatest tissue damage, and the most frequent incidence of localisation in body organs, systems and tissue.

Brucellosis in animals

Clinical features

The course of brucellosis in animals is sub-acute or chronic. The initial phase following infection is often unapparent, and the clinical signs are not pathognomic. In most host animals, abortions in the latter part of pregnancy, premature births and retained placenta are characteristic but not specific signs. The interference with fertility is usually temporary as most infected animals will abort only once, or have no abortion. The infection localises itself in the reproduction system and typically produces placentitis in females and epididymitis and orchitis in males.

Diagnosis

Infections acquired in utero or when sexually immature may be negative to serological testing until the animal aborts (*Madkour M., 2001*). Thus, the identification of one or more infected animals is enough evidence for the presence of brucellosis in the herd. Other serologically negative animals may present a risk as they might incubate the disease.

In view of the fact that clinical signs of brucellosis are not pathognomic, or may be absent, laboratory procedures are necessary. There are two categories of diagnostic tests, one demonstrating the presence of the organisms using some culture methods, and the other detecting an immune response to its antigens in serum. The later is, in practice, more feasible, but provides only a provisional diagnosis. For definite proof of the infection, the isolation method of *Brucella* is required. This may also be useful to monitor the progress of a vaccination programme. Unfortunately, the facilities needed are not always available, and the definite identification can only be made using techniques available at Brucella Reference Centres (*Corbel M. et al, 2000*).

Treatment

Economic losses occur in reproductive efficiency, in livestock commerce, and in animal replacement costs. But in most cases, treatment is not an option due to costs of therapy, antibiotic residues in milk, and high failure rates (*Madkour M., 2001*).

Transmission between animals

The organisms are shed out through the urine, milk or placenta fluid, thus potentially spreading at alarming rates. As pasture areas or accommodations may be contaminated, the bacteria are most frequently ingested, but they can be inhaled, spread by conjunctival inoculation and skin contamination as well. Sexual transmission plays a particularly important role in transmission of *B. melitensis* and *B. suis*. The transmission of diseases is facilitated by factors such as commingling of herds of different

owners, close contact caused by high flock density, and by purchasing unscreened animals. *Brucella* species are host specific to some extent, however cross-species infections occur: dogs can be infected with *B. abortus*, *B. melitensis* or *B. suis*, by ingesting ruminant foetal or placental material, and can then excrete bacteria and present a serious hazard to humans and domestic livestock (Corbel M. et al, 2000). Cattle can be infected with *B. melitensis* or even *B. suis* through close contact with small ruminants or swine herds (Poester F P et al, 2002) (1st International Conference on Emerging Zoonoses, 1997).

Brucellosis in humans

Transmission to humans

Brucella spp. can survive for long periods in dust, soil, slush, water, dung, aborted foetuses, meat or dairy products, and enter the human body through several ways varying according to the endemic situation (Madkour M., 2001). In endemic areas it is usually transmitted to humans through food.

Other modes of infection are respiration, cutaneous contact, the conjunctival contact or auto-inoculation. Transmission of *Brucella* organisms through inhalation commonly occurs among shepherds, animal handlers, farm workers, slaughterhouse workers and butchers, veterinarians and laboratory workers. Other risks among slaughterhouse workers are transmission through skin abrasion or accidental skin penetration. Veterinarians risk infection through accidental splash of live *Brucella* vaccines into the eyes or the accidental self-injection of live *Brucella* vaccines. Transmission of *Brucella* organisms from human to human is extremely rare.

Clinical features

Human brucellosis is an acute or sub-acute febrile illness marked by an intermittent or remittent fever (“undulant fever”). The most frequent clinical symptoms beside fever are chill or shaking, malaise, generalised aches and pains, joint and low back

pain, headaches, anorexia, tiredness, general weakness and mental depression (*Madkour M., 2001*). During systemic spread, the *Brucella* organisms disseminate widely from regional lymphoid tissue and may localise in lymph nodes, spleen, liver or bone marrow. Thus, human brucellosis is a disease with varied clinical manifestations and may simulate other diseases. In the absence of specific treatment human brucellosis may persist and progress to a chronically incapacitating disease with severe complications.

Incubation period

In about half of the cases brucellosis is acute, with an incubation period of two to three weeks. In the other half, the onset is insidious, developing over a period of weeks to months from the infection. The incubation period may vary according to the virulence of the organisms, the route of entry and the infecting dose (*Madkour M., 2001*).

Diagnosis

The diagnosis of human brucellosis is based on the history of exposure to a known or probable source of *Brucella*, the history of features of the disease at its onset, and significantly raised or rising *Brucella* antibody titres with or without positive cultures from blood or other fluids or tissues (*Madkour M., 2001*). Due to the extraordinary variety of manifestations of this disease, the diagnosis cannot be made solely on clinical grounds. The Rose Bengal Test (RBT) can be used as the most sensitive rapid screening test, but the results must be confirmed by bacteriological and other serological tests (*Corbel M. et al, 2000*). However, the presence of antibodies does not always mean an active case of brucellosis. In endemic areas, sub-clinical infection with *Brucella* organisms may lead to the presence of a high titre of *Brucella* agglutinins in an otherwise asymptomatic individual. In endemic areas, a titre of 1:640 is significant, while in non-endemic areas a titre of 1:160 is significant (*Madkour M., 2001*). Therefore, there are no agreed unified agglutination titre levels which can be considered significant and indicative of active brucellosis.

Treatment

The essential element in the treatment of all forms of brucellosis is the administration of effective antibiotics, and treatment should be implemented at an early stage. Treatment regimes usually consist of combination of at least two agents; however, the optimum antibiotic therapy is still disputed (*1st International Conference on Emerging Zoonoses, 1997*). The full treatment lasts 7 to 12 weeks. A shorter duration of treatment is associated with higher relapse rates. Additionally, severely ill patients should be treated in a hospital. In those patients with complications, additional treatment is necessary including, in some cases, surgical intervention.

2. Worldwide spread of Brucellosis

There is no worldwide, coordinated and comprehensive reporting on the spread of brucellosis and therefore there are no statistics available or published. This thesis's overview on the burden of brucellosis in the different parts of the world has been assembled by reviewing the literature and choosing the most robust available data. Some of this data were overviews supplied by the O.I.E. and FAO, and surveys and conference notes on the spread of brucellosis provided by literature search through the internet. This results in the maps shown in the *figure 2.1.* of worldwide brucellosis distribution. The template map has been downloaded from internet⁴.

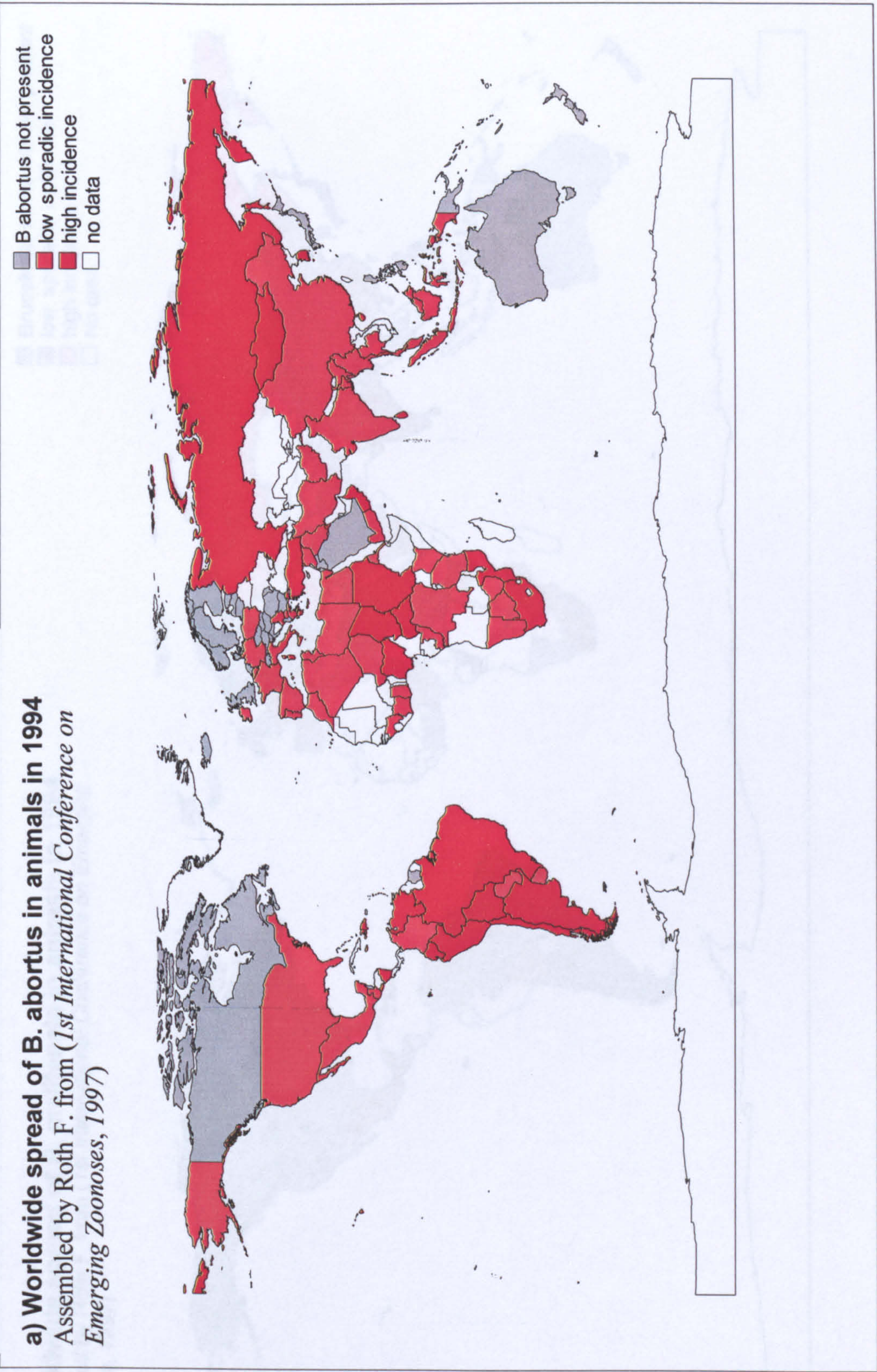
The database for the spread of *B. melitensis* and *B. abortus* were culled from a 1994 report on the First International Conference on Emerging Zoonoses (*1st International Conference on Emerging Zoonoses, 1997*). The incidence is shown in broad categories: (i) not present or eradicated, (ii) low sporadic incidence, (iii) high incidence and (iv) no data.

⁴ <http://www.rbgekew.org.uk/gis/tdwg/index.html>

The maps concerning animals show that *B. abortus* is more spread out worldwide than *B. melitensis*, - the latter remaining the principal cause of human brucellosis. The third map aggregates the burden of *B. abortus* and *B. melitensis*.

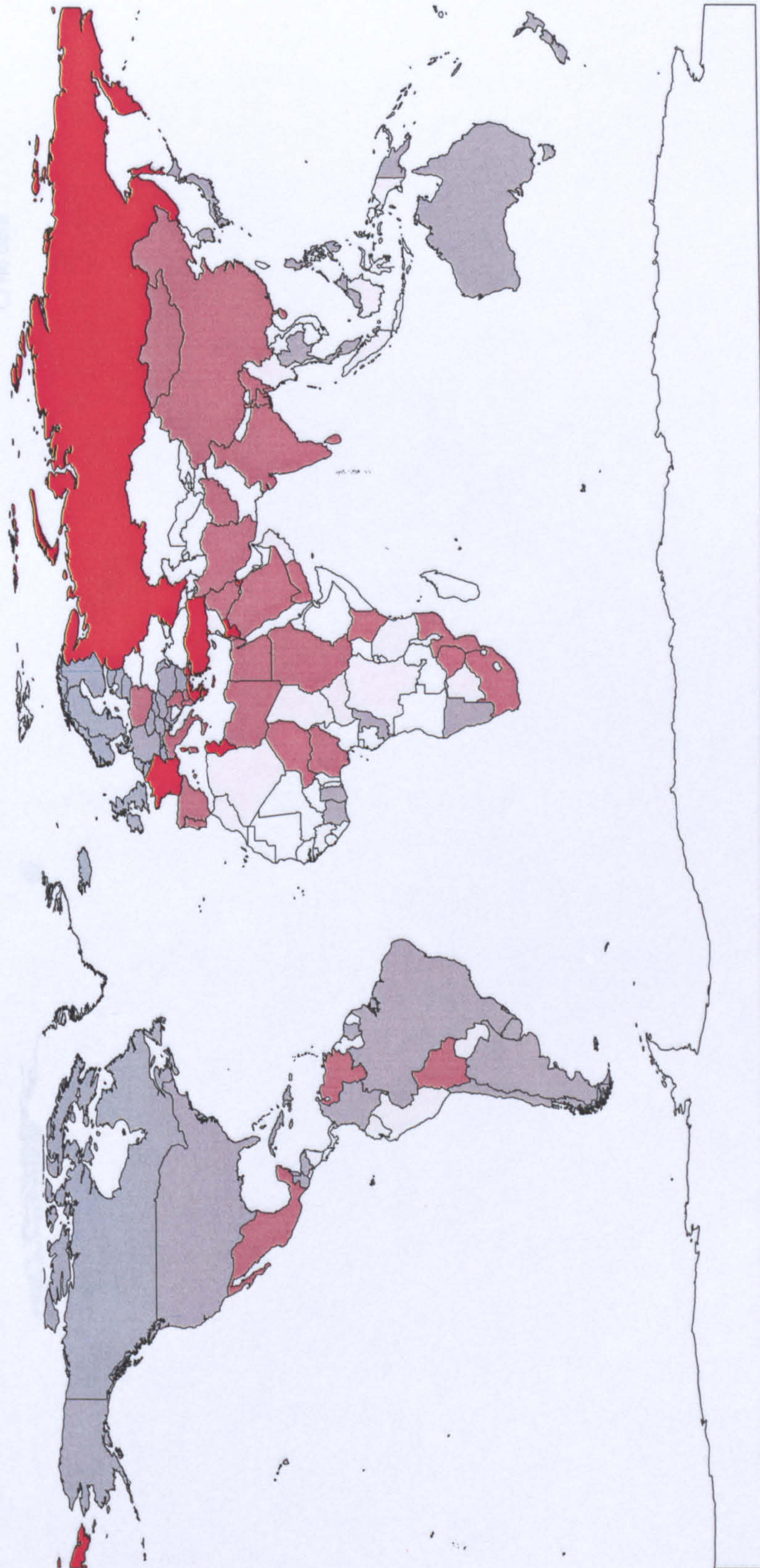
This analysis considered only *B. abortus* in cattle and *B. melitensis* in sheep and goats, as this was relevant for the further search of the brucellosis epidemiology in Mongolia. However, the following species affected by brucellosis worldwide are: cattle, sheep, goats, pigs, and with a lower importance: bison, camels, dogs, horses, reindeer, yaks and marine mammals (*Corbel M. et al, 2000*).

Figure 2.1.: Worldwide spread of Brucellosis

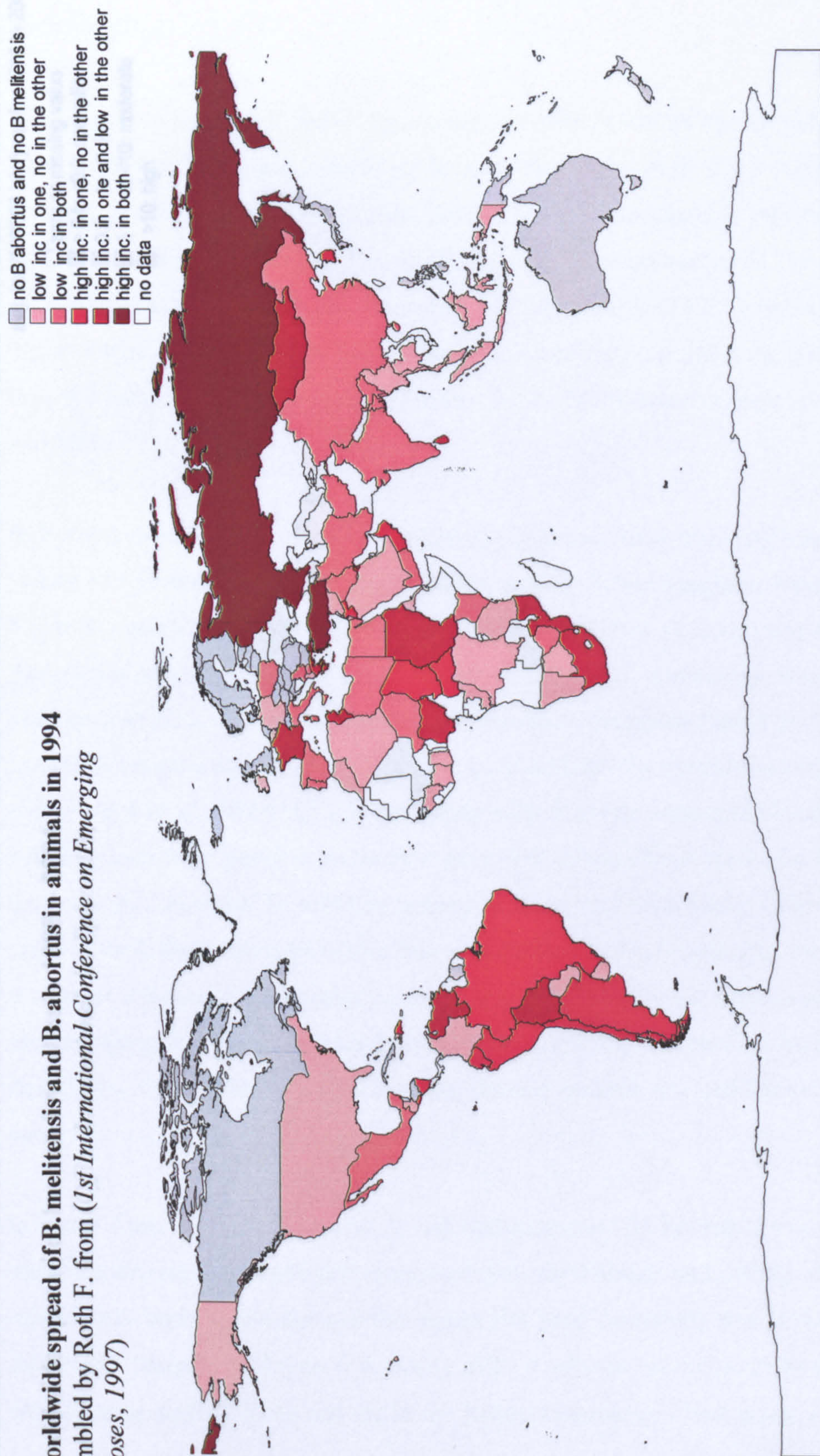


Brucellosis melitensis not present
 low sporadic incidence
 high incidence
 No data

b) Worldwide spread of *B. melitensis* in animals in 1994
 Assembled by Roth F. from (1st International Conference on Emerging Zoonoses, 1997)



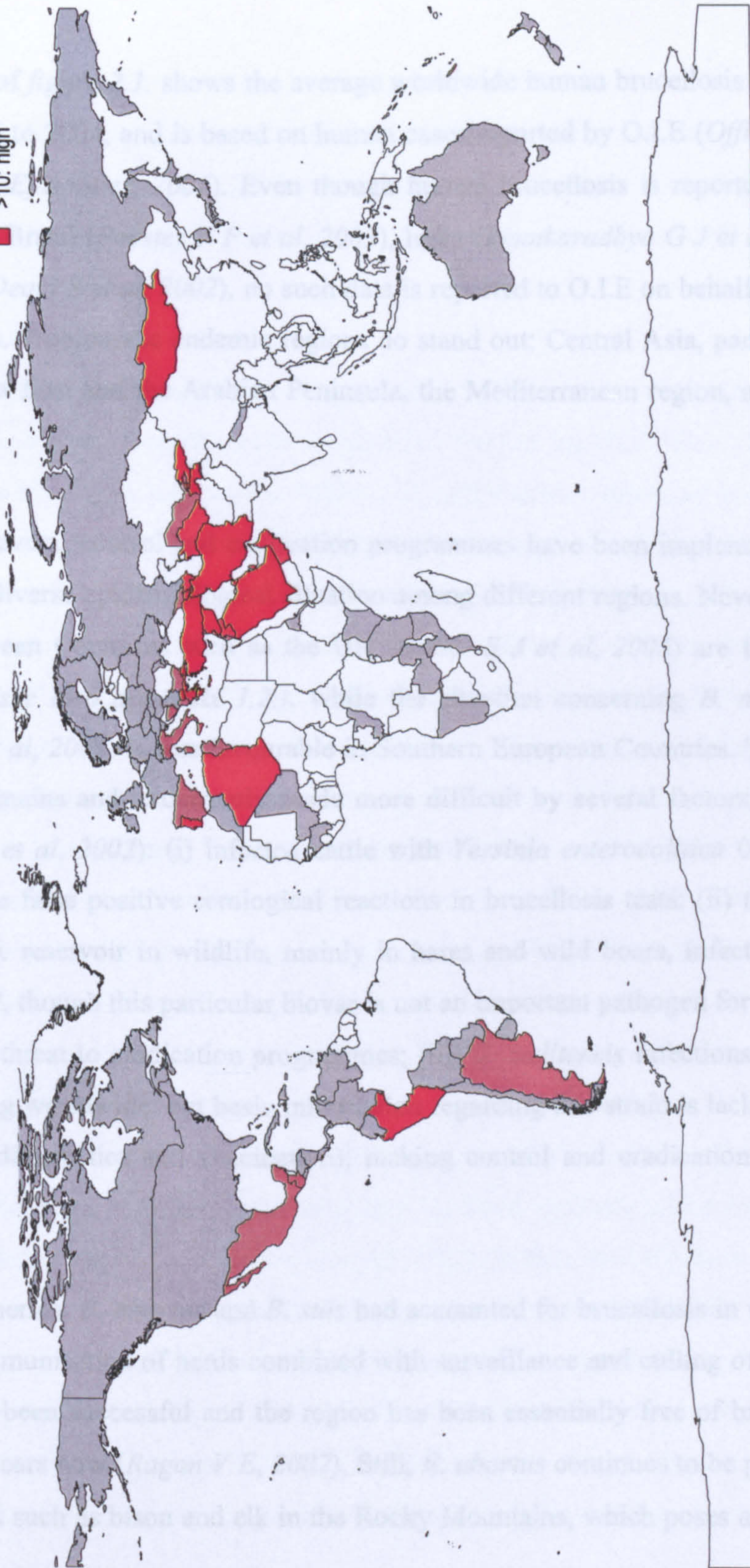
c) Worldwide spread of *B. melitensis* and *B. abortus* in animals in 1994
 Assembled by Roth F. from *(1st International Conference on Emerging Zoonoses, 1997)*



d) Worldwide spread of human brucellosis 1996 – 2004
 Assembled by Roth F. from (*Office International des Epizooties*, 2005)

avg. inc./100'000 inh./year for 1996 to 2004

- zero or missing value
- > 0 to <0.6: sporadic
- 0.6 to <3: low
- 3 to <10: moderate
- >10: high



Data that were more than ten years old have been included because there is little data on the topic.

The map d) of *figure 2.1.* shows the average worldwide human brucellosis distribution for 1996 to 2004, and is based on human cases reported by O.I.E (*Office International des Epizooties*, 2005). Even though human brucellosis is reported in the literature for Brazil (*Poester F P et al*, 2002), India (*Renukaradhya G J et al*, 2002) and China (*Dequi S et al*, 2002), no such data is reported to O.I.E on behalf of these big countries. Problematic endemic regions do stand out: Central Asia, parts of Africa, the Near East and the Arabian Peninsula, the Mediterranean region, and Latin America.

In Europe, several control and eradication programmes have been implemented resulting in a diverse epidemiological situation among different regions. Nevertheless, North European Countries such as the UK (*Cutler S J et al*, 2005) are free from brucellosis (*see also appendix 1.2.*), while the situation concerning *B. melitensis* (*Taleski V et al*, 2002) is less favourable in Southern European Countries. Thus, the challenge remains and is currently made more difficult by several factors, such as (*Godfroid J et al*, 2002): (i) infected cattle with *Yersinia enterocolitica* 0:9 (Y09) which induce false positive serological reactions in brucellosis tests; (ii) there is a *Brucella spp.* reservoir in wildlife, mainly in hares and wild boars, infected by *B. suis* biovar 2, though this particular biovar is not an important pathogen for humans, it remains a threat to eradication programmes; (iii) *B. melitensis* infections in cattle are increasing worldwide, but basic information regarding this strain is lacking (epidemiology, diagnostics and vaccination), making control and eradication difficult too.

In North America, *B. abortus* and *B. suis* had accounted for brucellosis in most animals, but immunisation of herds combined with surveillance and culling of infected animals has been successful and the region has been essentially free of brucellosis for several years now (*Ragan V E*, 2002). Still, *B. abortus* continues to be present in wild animals such as bison and elk in the Rocky Mountains, which poses a threat of

infection to cattle, or reindeer in Alaska, accounting for occasional human cases (Rust R S, 2004).

Historically, *B. abortus* was endemic in cattle herds in New Zealand and Australia, but a successful animal vaccination and surveillance campaign resulted in eradication in both countries by 1989 (Miller M et al, 2005) (Crump J A et al, 2001). *B. melitensis* is absent in animals in most parts of these countries, though a few human cases occur.

In Latin America, brucellosis is mainly reported in the context of cattle farming, where beef production contributes to a significant part of the GDP (Baumgarten D, 2002). As the economic impact of brucellosis is considerable, important investments have been made towards efforts to control this disease, as reported from Chile (Rivera S A et al, 2002), Argentina (Samartino L E, 2002), Paraguay (Baumgarten D, 2002), Brazil (Poester F P et al, 2002), Venezuela (Francisco J et al, 2002), Central American States (Moreno E et al, 2002) and Mexico (Luna-Martínez E J et al, 2002). Brucellosis in sheep and goats is considered a disease of minor importance, with the exception of Mexico and the Andes States (Peru) (WHO et al, 2005). Human infection is considered to be underestimated as the reporting and diagnostic services for human brucellosis are inadequate (Poester F P et al, 2002). An underreporting rate is published for Mexico, where the real notification rate of human cases is estimated at 30% (Luna-Martínez E J et al, 2002).

In sub-Saharan Africa, brucellosis remains mainly a neglected disease with little attention to control and prevention (Smits H L et al, 2004), except in the southern African region, where successful control policy has been reported in Botswana, Zimbabwe and South Africa (McDermott J. et al, 2002). In fact, brucellosis is prevalent in most sub-Saharan livestock production systems, common in cattle and perceived to a lesser level in small ruminants. This is not only the consequence of lack of awareness by both veterinarians and health care staff but also to the absence of accessible laboratory diagnostic facilities. The difficulty in diagnosing brucellosis in humans without laboratory testing is due to the similarity with clinical presentations

of other infections occurring in sub-Saharan Africa such as malaria. The situation in the animal sector is similar as the cause of abortions is confounded with other common animal diseases present in Africa (*Zinsstag J. et al, 2004*).

In countries of the Near East region and the Arabian Peninsula, brucellosis infection has had a long history (*WHO, 2005b*), due to the traditional consumption of raw milk and milk products (*Awed R, 1998*). The disease is considered a major risk for humans; 40,000 new human cases are reported every year and the true infection rate is probably higher. Brucellosis often remains unrecognised and is treated in the same fashion as other diseases, labelled “fever of unknown causes”. Most human infections are due to *B. melitensis*, which can be transmitted by almost all domestic animals. There is a rising awareness concerning the importance of controlling brucellosis in animals; most countries have already attempted to control it, some with good results, while others do little (*Refai M, 2002*).

There is a low sporadic incidence of brucellosis over the Asian continent (*Bandara A B et al, 2002*). Areas of highest incidence in the region are Sri Lanka (*Bandara A B et al, 2002*) and the Indian subcontinent (*Renukaradhya G J et al, 2002*). Remarkably neither of these countries has ever controlled brucellosis. It is not present in the animals of Malaysia (Sabah), the Philippines and Japan (*1st International Conference on Emerging Zoonoses, 1997*). In former USSR-Countries and Central Asia brucellosis is a serious and longstanding problem in livestock and humans. China has a longstanding experience with brucellosis control, especially in provinces where stock raising is important, with the dominant strain being *B. melitensis*. Also Inner Mongolia has suffered from severe epidemics before the 1980s and has suffered again since the 1990s. (*Dequi S et al, 2002*). China has established control programmes since the 1950s, with comprehensive measures based on studies of the infection sources and transmission modes. Methods employed were quarantine, separation and elimination of infected animals and also immunisation campaigns, starting in the late 1950s (*Dequi S et al, 2002*). Nevertheless, brucellosis remains a serious public health issue.

3. Mongolia's situation in an international context

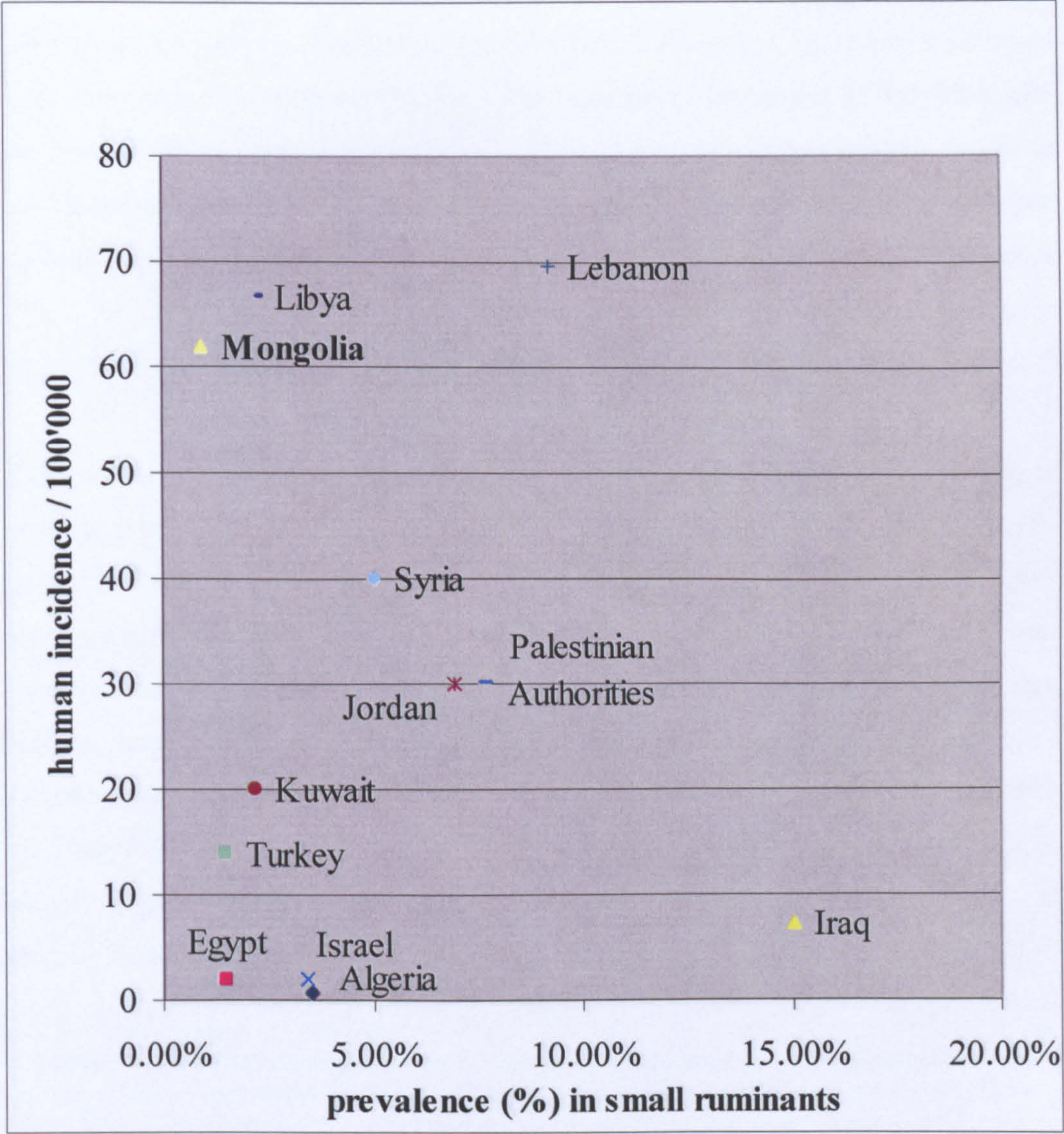
The main risk of infection is different in the non-endemic areas, where the source of infection is mostly work-related (veterinarians, abattoir workers and laboratory personnel), from the risk of infection in the endemic areas, where the infection is mainly related to hygienic methods and community eating habits (consumption of raw food such as contaminated raw milk or un-pasteurised cheese) (*Araj G F, 1999*). To analyse the animal to human transmission we need to quantify the relation between disease reservoir in the animals and new infections in humans. The most comprehensive data available in an international context concerns the Near East region, which is one of the most contaminated regions of the world. The review article of M. Refai (*Refai M, 2002*) tries to assess brucellosis in man and animals in the region, while mindful of the lack of information. In fact, besides using publications, M. Refai depended on data he accumulated during FAO/WHO consultancy missions through seminars, workshops and country reports. In the following analysis, the human incidence is put in relation to the prevalence of *B. melitensis* in SR, as this strain is the predominant cause of brucellosis in humans⁵ (*Refai M, 2002*) (*Awed R, 1998*).

The data extracted out of this review for our purpose are plotted in the *figure 2.2*. The negative binomial regression analysis showed a significant correlation (LRT = 12.58, P-value = 0.0004) between the prevalence in animals and the incidence in human for these countries of the Near East Region. Despite all limitations, such as poor data quality, different study designs, different observation years etc., we can statistically establish what is known: the disease incidence in humans closely parallels animal prevalence, although the likelihood of disease in human is further greatly influenced by the degree of contact with animals and their excreta, or the ingestion of animal products (*Rust R S, 2004*). Thus, by adding the corresponding data of

⁵ *B. melitensis* infecting cattle can not be considered as there are no data available distinguishing the infection in cattle between *B abortus* and *B. melitensis*.

Mongolia in *figure 2.2.*, we see that Mongolia takes an “outlier position” because of its lowest brucellosis prevalence in animals combined with very high incidence in humans (even compared with Near East countries, representing one of the most contaminated region of the world!). This is important to consider for choosing and applying surveillance policies, such as testing methods (specificity of the tests) and prevention measures. Compared to other countries, there seems to be an extremely close animal-human contact in Mongolia, which could be due to its nomadic livestock rising, where both transmission routes (the work related and the alimentary) have to be considered at the same time.

Figure 2. 2: Brucellosis prevalence in small ruminants and incidence in humans: situation in the Near East (1984–1999) and Mongolia (1999)



Material out of (Refai M, 2002) for Near East Region and (National Statistical Office of Mongolia, 2003) (Health Development Centre, Mongolia, 2002) (Ministry of Agriculture, 2003c) for Mongolia

4. Brucellosis control

The first section of this chapter described the characteristics of brucellosis and showed that most human brucellosis originates from an infected animal. Human to human infection is rare. Prevention includes health education and pasteurisation of milk. However, education campaigns alone have never succeeded in fully eliminating these risks to humans (*Robinson A, 2003a*). Attempts at vaccinating people at risk have resulted in effective protection, but also provoked severe reactions when given to sensitised individuals, or when administered incorrectly (*Schurig G G et al, 2002*). As a result, vaccination of humans is no longer routinely used⁶; the ultimate prevention of human infection remains the elimination of the brucellosis in animals.

This section describes the measures to control, eradicate and prevent brucellosis in animals. It provides the basis for understanding and analysing Mongolia's brucellosis control policy, described in chapter 5. Currently, methods used to prevent infections are *test and slaughter* (T&S) of seropositive animals, *vaccination*, *hygiene measures*, and *management*. Various factors influence the choice of methods used such as husbandry system, climate, nomadic livestock breeding, prevalence of brucellosis among various animal species, and control programme resources available. As clinical signs are not evident, testing is crucial to estimate the prevalence of brucellosis. Therefore, the details of methods will be preceded by an overview of brucellosis tests.

⁶ "Renewed interest in *Brucella* as a potential biological warfare agent has ...drawn attention to the need for effective vaccines for humans. ...The cost implication and limited commercial possibilities for vaccines against human brucellosis mean that development is likely to be restricted to national defence agencies." (*Schurig G G et al, 2002*)

Brucella species are considered by the CDC (*Centers for Disease Control and Prevention, 2000a*) to be Category B biological warfare agents, which are the second highest priority agents. The biological warfare route of infection is most likely aerosol. Category B agents are moderately easy to disseminate, cause moderate morbidity and low mortality, and require specific enhancement of diagnostic capacity and enhanced disease surveillance. Additionally, brucellosis is listed among critical biological agents as having disease characteristics with particular potential for biologic terrorism (*Centers for Disease Control and Prevention, 2004*). To ensure a prompt response to a biological terrorist event, early detection is essential. However, this is difficult in a population with a low prevalence of disease, as to rule out false-positive laboratory findings, diagnostic laboratory testing has to be integrated with lengthy epidemiologic investigation (*Centers for Disease Control and Prevention, 2000b*).

Testing

Brucellosis can be diagnosed only by isolating and identifying the causative organism, *Brucella* spp. But this is not possible in the field as techniques for this are only available at Brucella Reference Centres (*Corbel M. et al, 2000*). Therefore, the most practical diagnosis of brucellosis involves an indirect test using antibody specific tests in serum or milk. Serological diagnosis can be unclear, as vaccines may be serologically indistinguishable from virulent strains, and cross-reaction with other agents may occur. This leads to diagnostic dilemmas. With the development of an assay, vaccination antibodies could be distinguished from antibodies resulting from field infection. But the acceptance of these serological tests has been slow (*Nielsen K, 2002*). The same tests are applicable to animal and human serology.

A number of tests have been developed for brucellosis (*see figure 2.3.*). A test with higher sensitivity misses fewer false negatives. A test with higher specificity will result in fewer false positives. This has to be considered according to the circumstances applied and the stage achieved in the process of controlling and eradication of the disease. At the beginning of a control programme, when broad screening is carried out to get an overview of the spread of disease, sensitivity of a test is most important. When eradication is progressing, then the specificity of a test becomes crucial to obtain a precise view on the residual elements of disease and identify the individual carrier of pathogens. After eradication it is important to monitor changes in the situation and investigate particular problem herds or areas; for this a test with good sensitivity should be used again. *Table 2.3.* lists the sensitivity and specificity values for various serological tests and shows that no individual test is perfect.

Predicted value positive indicates the probability a case is infected given a positive test result (right positive). Analogously, predicted value negative indicates the probability a case is not infected given a negative test result (right negative). Increasing the specificity of a screening test (by changing the criterion of positivity) increases its predictive value positive. The predictive value positive of a screening test can

Figure 2.3.: Diagnosis of brucellosis by serology

Sensitivity, specificity, and performance index of the serological tests for brucellosis

Test	Sensitivity ^a	Specificity ^a	Performance index ^a	References
SAT	29.1–100	99.2–100	129.1–200	Van Aert et al., 1984; Lord et al., 1989
RBT	21.0–98.3	68.8–100	121.0–193.9	Van Aert et al., 1984; Samartino et al., 1999
Card	74.3–99.0	7.4–100	106.4–187.5	Stemshorn et al., 1985; Huber and Nicoletti, 1986; Lord et al., 1989
BPAT	75.4–99.9	90.6–100	174.3–199.7	Stemshorn et al., 1985; Uzal et al., 1996; Samartino et al., 1999
RIV	50.5–100	21.9–100	108.7–200	Huber and Nicoletti, 1986; Lord et al., 1989; Dajer et al., 1999
2ME	56.2–100	99.8–100	156.2–200	Lord et al., 1989; Stemshorn et al., 1985; Saravi et al., 1995
CFT	23.0–97.1	30.6–100	123.0–197.5	Huber and Nicoletti, 1986; Van Aert et al., 1984; Saravi et al., 1995
PCFIA	92.0–98.1	48.6–69.9	140.6–168.0	Nicoletti and Tanya, 1993; Nielsen et al., 1998
IELISA	92.5–100	90.6–100	190.9–200	Dohoo et al., 1986; Rojas and Akonso, 1994
CELISA	97.5–100	99.7–99.8	197.3–199.8	Samartino et al., 1999; Nielsen and Gall, 2001
FPA	99.0–99.3	96.9–100	195.9–199.3	Dajer et al., 1999; Nielsen and Gall, 2001

^a Sensitivity and specificity values are presented as percent ranges of the worst and best results. The literature cites for each test with very low results used sensitivity and specificity calculations relative to other serological tests while the higher values were obtained using sera from cattle from which *B. abortus* was cultured or experimentally infected animals. The performance index is the sum of the % sensitivity and specificity.

(Nielsen K, 2002)

also be increased by increasing the prevalence in the screened population (targeting to groups with high risk) (Hennekens C H et al, 1987). Therefore, a combination of tests has to be applied, according to considerations such as budget restrictions, technical possibilities, and need for sensitivity or specificity. Tests can be administered either in parallel or in series, whereas parallel testing increases generally the sensitivity, and serial testing increases the specificity (Hennekens C H et al, 1987). Therefore, an appropriate testing procedure for brucellosis is serial testing. The test first applied should have a high sensitivity, detecting all positive samples and leaving only true negatives. The first test should ideally be inexpensive and easy to administer, and may be weak in specificity. From the first run, only positive samples are kept for the second run, which should have a high specificity and exclude false positives. This procedure can reduce costs since as the second more specific test may be more complex and costly (Honhold N., 1994b).

In most brucellosis control situations, the entity of interest should be the infected flock or herd rather than the infected individual animal (*Food and Agriculture Organisation of the United Nations Rome, Italy, 1992*). Whatever testing is applied it is impossible to detect all infected animals at a particular time; hence, the entire flock should be regarded as infected even if only one animal proves to be positive. Each infected flock poses a risk for public health (*Garin-Bastuji B., 1999*): Human cases may often be a useful indicator of the presence of the disease in animal populations or may sometimes be the only source of information for surveillance (*Corbel M. et al, 2000*).

The following tests are suitable for herd surveillance: (i) the Milk Ring Test (MRT): a relatively insensitive agglutination test, appropriate only for locating infected dairy cattle herds (*World Health Organization et al, 1986*); (ii) The Allergic Skin Test (AST), a more promising method for detecting infected herds of sheep and goats. It involves only minimum handling of the animals, and an individual animal identification is not required.

The following tests are widely applied for diagnosing individual animals: (i) The Rose Bengal Test (RBT), a standardised spot agglutination test, simple to perform and inexpensive. However, there are conflicting opinions on the efficiency of this test in detecting infected animals (*World Health Organization et al, 1986*). As most agglutination tests, RBT is susceptible to false positive reactions (or oversensitive) due to cross-reactions⁷ and vaccine titres in *Brucella*-vaccinated animals (*Nielsen K, 2002*). To confirm reactors it is therefore necessary to apply another test. (ii) The Serum Agglutination test (SAT), a simple test, but many studies have reported a poor sensitivity as well as specificity (*World Health Organization et al, 1986*). (iii) The Complement Fixation Test (CFT), recognised as the most reliable and effective test for diagnosing brucellosis in individual cattle, sheep and goats (*World Health Organization et al, 1986*). As it is associated with a high work load, and the procedure is technically complex, its worth lies in the use for confirming positive reactors

⁷ with *Y. enterocolitica* O9-infected animals and animals with other Gram-negative bacteria (*Erdenebaatar J et al, 2004*)

found in preliminary screening tests. (iv) New generations of tests with Enzyme-Linked Immuno-Sorbent Assay (ELISA) based on the characterisation of diagnostic antigen (DNA), knowledge of the host immune responses, and use of specific antibody reagents (*Food and Agriculture Organisation of the United Nations Rome, Italy, 1992*). These tests aim to overcome most of the drawbacks associated with conventional techniques of serological tests; they improve both sensitivity and specificity, implement a high level of international standardisation, and discriminate responses due to immunisation or exposure to cross-reacting organism from field infection.

In Mongolia, tests used must be simple, quick and cheap. Although sensitivity might be lower, experiences in developing countries have shown that simple screening tests (such as card agglutination test with buffered antigen) meet most diagnostic needs (*Kolar J., 2001*). A further test helpful for brucellosis surveillance in nomadic conditions is the allergic skin test (*Kolar J., 2001*). For specification or verification of doubtful results, serological quantitative tests such as SAT or CFT are helpful (*Kolar J., 2001*). Also, recent studies in Mongolia demonstrated good results when combining RBT for screening and ELISA tests with sarcosine extracts for confirmation (*Erdenebaatar J et al, 2004*). ELISA could discriminate positive results in such cases. Further, ELISA with sarcosine extracts proved to be more convenient for practical applications than CFT, and a more useful confirmatory test in the Mongolian context.

Test and Slaughter

The following steps are usually applied in T&S programmes, where animals are tested for evidence of antibodies to brucellosis and positives are separated from other animals (*Madkour M., 2001*): (1) identification of the susceptible animals, for example with ear tags; (2) performing serum tests, (3) removal of seropositive animals for isolation or slaughtering; (4) retesting remaining animals, until herd tests are negative for at least 6 months; (5) purchasing new animals from brucellosis-free

populations only; (6) keeping herds under surveillance. T&S is based upon the fact that infected animals can be contagious throughout their life-time while not showing pathognomic signs. If possible, infected animals should be removed from the population prior to parturition, when transmission occurs. T&S has been successful in situations where farms and herds are small, and where there is little movement of livestock.

T&S is often ineffective in large populations as animals, tested positive with serological tests, may have spread *Brucella* by the time they are identified. One problem is that up to 20% of infected cattle do not show blood antibodies, until after they abort. It is during abortion that transmission risks are highest, when billions of organisms are spread (*Honhold N., 1994b*). Only few countries have been able to eliminate brucellosis in sheep and goats through T&S. In nomadic settings, the limitations of T&S are most revealed by the great size and movement of the herds, the poor logistics of test administration, the lack of sufficient funds for programme administration and for financial compensation to owners. The separation of the infected animals has to be enforced by government regulations, and slaughtering within a certain period after testing (2 weeks) has to be compulsory. The prerequisite of this is an accurate identification tool, and the use of a compensation scheme is essential to ensure the owners' co-operation.

Vaccination

T&S is not realistic in the majority of places where *B. melitensis* is endemic (*Banai M, 2002*). Therefore, until the disease prevalence is significantly reduced, whole herd immunisation should precede T&S activities. Experts advise a shifting away from immunisation to a T&S policy only after the individual prevalence rate is no greater than 2-3% and the herd prevalence is 5-10% (*Food and Agriculture Organisation of the United Nations Rome, Italy, 1992*).

Vaccine protection from infection is not absolute and to achieve high vaccination coverage, animal owners have to give their consent and a vaccine campaign has to be backed up with sufficient regulatory authority and resources. Furthermore, the correct administration of vaccines is crucial to develop rapidly a herd's resistance.

The vaccines have been initially developed on an empirical basis, and their administration was based on trial experience and was subject to continuous evolution (see chapter 5). The current research on brucellosis vaccine attempts to stimulate a protective immune response by introducing genes encoding protein antigens (DNA vaccines) (Schurig G G *et al*, 2002). But these recent attempts have been hindered by an incomplete knowledge of the protective antigens of *Brucella* (Schurig G G *et al*, 2002)⁸.

The most successful vaccines used so far for the immunisation of farm animals were S19 and Rev.1. Both used live smooth attenuated derivatives of *Brucella spp.*, S19 of *B. abortus* and Rev.1 of *B. melitensis*. S19 had been developed by Buck in late 1930th and protects cattle against *B. abortus* but not against *B. melitensis* (Kolar J., 1992). Depending on animal age, dose, and route of vaccine administration, antibodies appear and persist in serum, and prevent the differentiation of vaccinated from infected cattle. This makes the use of this vaccine incompatible with simultaneous T&S application (Schurig G G *et al*, 2002). In 1996, APHIS licensed the *B. abortus* Strain RB51 Vaccine, a live attenuated rough strain, which does not stimulate the production of antibodies on standard diagnostic tests (Lin D X *et al*, 2000). Primarily responsible for the immunisation is the production of a cell-mediated response. This vaccine has been implemented in the USA, Mexico and Chile, and replaced S19 (Schurig G G *et al*, 2002).

Rev.1 vaccine can be used also in cattle, where *B. melitensis* is prevalent in SR, and where it may be the cause of infection in cattle. The protection against *B. abortus* is

⁸ *Brucella* is found inside the cells rather than in the circulation. So, as the *Brucella* is therefore protected from antibodies, it is not the antibodies that protect the animals from infection by *Brucella* bacteria, but cell mediated immunity (Honhold N., 1994b).

comparable to protection provided by S19 (*Kolar J., 1992*), or even better (*Schurig G G et al, 2002*). However, because of fear of the risk of Rev.1 excretion in milk, epidemiologists resist the use of Rev.1, preferring instead S19 to fight *B. abortus* (*Banai M, 2002*). To obtain protection against *B. melitensis* infection, Rev.1 vaccination of cattle has been used in Mongolia (see chapter 5). The extension of this procedure to endemic areas is suggested (*Banai M, 2002*).

The Rev.1 vaccine is used for immunisation of SR against *B. melitensis*. "Rev.1 vaccine is a live, attenuated *B. melitensis* strain derived from a virulent *B. melitensis* isolate which became dependent on streptomycin for its growth, but lost this characteristic, although remaining streptomycin resistant, upon further subculture" (*Elberg S. et al, 1956*) (*Schurig G G et al, 2002*). The Rev.1 strain has been isolated by Prof. S. Elberg⁹, and has been intensively studied since 1955 in several countries worldwide, and was proven to protect SR in endemic areas. Like the S19 vaccine, the vaccine Rev.1 also induces positive serology, preventing the differentiation between vaccinated and infected animals. However, this interference could be reduced by shifting from subcutaneous administration to the ocular method (conjunctival administration) (*Banai M, 2002*).

This leads to an important topic of this thesis: in the late 1960s and 1970s local production of the Rev.1 vaccines had been established for local use. The vaccine became the basis of several national control programmes, such as in Italy, Iran, Israel, USSR, Turkey, South Africa, Peru and Mongolia (*Elberg S., 1981*). Later on, in late 1970s and 1980s, Rev.1 vaccination of SR became an important pillar in the control programmes in France, Greece, Spain and Kuwait as well (*Elberg S., 1996*). The control programmes, and the use of Rev.1, varied between these countries, but no conclusion regarding the success or failure of these immunisation campaigns could be reached, as the results were not obvious (*Banai M, 2002*). Chapter 5 looks into the 1970s Mongolian large-scale immunisation programme, which is considered to be one of the most successful (*Elberg S., 1996*). It eventually became one of the world's largest immunisation campaigns using Rev.1 in SR, vaccinating about 33

⁹ Sanford S. Elberg, School of Public Health, University of California, Berkley, USA

million of them. Only one other vaccination programme was larger: in the Central Asian Republics of the USSR several hundred million SR were vaccinated with Rev.1 (*Elberg S., 1996*).

Management practices

Hygiene methods or management practices can be applied to reduce exposure of susceptible animals and reduce exposure to their discharges and tissues. As diagnostic tests in individuals are not sufficiently reliable to assure the absence of disease, animal replacements have to be purchased from herds that are certified *Brucella*-free. Commingling with herds of unknown status should be prevented and animals should be isolated at parturition to prevent possible transmission of infection. All these measures aim to reduce exposure, but may be difficult to put into action in nomadic conditions.

5. Key thoughts on Brucellosis

Despite powerful approaches provided by technical improvements during the last decade, the understanding of the *Brucella* pathogenesis still remains in its infancy and the scientific community is far from understanding the molecular mechanisms of *Brucella* and how this bacteria causes brucellosis (*Letesson J J et al, 2002*). Developments in radiological and laboratory diagnostic methods have contributed to advances in information about the effect of the disease on every organ of the human body. Therapy, however, has not kept pace with these advances. In treating patients with brucellosis, relapses and therapeutic failure still constitute the major problems (*Agalar C et al, 1999*) (*Ariza J et al, 1995*).

Factors contributing to the rising spread of brucellosis in animals are related to the recent expansion of the animal industry (*Madkour M., 2001*). Three new develop-

ments in the epidemiology of brucellosis challenge control policies (*Maurin M, 2005*): (i) the reservoir of brucellosis in wildlife is expanding, possibly impacting on domestic animals; (ii) cattle are infected by *B. melitensis* but vaccines are not yet well-established for this constellation; and (iii) a disease reservoir has been recognized in marine mammals, and their potential virulence to humans remains unknown.

Brucellosis can impact more deeply on poorer communities (*Perry B D et al, 2002*). As surveillance of brucellosis needs huge financial investments, it is not uncommon to encounter large – scale efforts to control the disease where large-scale cattle and sheep husbandry have an important economic role. This is the case in Latin American countries, the USA, New Zealand and Australia. These countries have succeeded in controlling or even eradicating *B. abortus*. However, the most difficult to control is *B. melitensis* (*Nicoletti P, 2002*), which is at the same time the most virulent species for humans. Commonly, regions infected are pastoral communities, in which sheep and goats play an important role and where husbandry practices create difficulties for the control of brucellosis. However, pastoralist systems account for only a small part (5%) of the rural poor, where the great majority of poor associated with livestock are found in mixed crop-livestock systems (*Perry B D et al, 2002*), common in developing countries endemic with brucellosis. The disease presents a constant threat to both reproductive performance amongst animals and human health. The development and application of suitable control strategies for these smallholder dairy systems would mean an important step in poverty alleviation through improved animal health.

1. Research question

The central research question addressed in this thesis is: “Is there any relationship between stated surveillance policy and the brucellosis prevalence in animals and the brucellosis incidence in humans?” Four aims provide investigative steps to address this question:

1. To establish epidemiological patterns of brucellosis in animals and humans in Mongolia from 1966 to 2002;
2. To provide an historical overview of the different strategies applied to the control of brucellosis in Mongolia;
3. To analyse the possible interactions between the strategies applied to control brucellosis and its spread;
4. To make recommendations about surveillance policies for brucellosis.

2. Type of information required and how it was obtained

Type of information required

The following information was needed for the analysis:

- (i) Information on the characteristics of brucellosis, its epidemiological aspects and methods of surveillance.

- (ii) To estimate the spread of brucellosis in Mongolia (aim 1), consistent and reliable data by year and by Aimag¹⁰ was required on the human incidence and animal prevalence.
- (iii) Information on the methods for control, eradication and prevention was required. (aim 2). The surveillance policy was defined for the whole nation, but implemented during different years at the Aimag level. So surveillance policy was needed on Aimag level. To understand the surveillance policies in their historical context, information on the political and economic situation was collected. To underpin this qualitative information quantitative data on production, vaccine use, and animal testing were collected.
- (iv) Information on the etiology of brucellosis was needed to understand and assess possible interactions between the strategies applied to control brucellosis and the spread of disease (aim 3).
- (v) Information on the worldwide spread of brucellosis in animals and humans, and the current efforts for control, eradication and prevention was needed, to inform surveillance policy.

How the required information was obtained

Information and data as described above were collected first in London, Prague, and Geneva. The field work in Mongolia searching paper and electronic records and interviewing key persons completed gaps of information and data required.

Paper and electronic records

This included electronic searches of databases for journals and catalogues of libraries, searching the internet and searches in the intranet of WHO headquarters. Non-electronic searches were conducted in various archives such as at WHO Geneva and authorities in Ulaanbaatar. Other documents were located after discussions with par-

¹⁰ An Aimag is the primary administrative unit in Mongolia, i.e. province; it consists of several Soums

ticipants at the Brucellosis 2003 International Conference in Spain, through interviewing key persons and by searching through the files of experts.

Networks of informants

A network of brucellosis experts resulting from the previous study¹¹ was reactivated. The contact with Dr. O. Cosivi¹² was crucial, facilitating access to the knowledge based at WHO headquarter. The richest source of information was gained from network of key experts in Mongolia. The collaboration with Dr. J. Kolar¹³ was outstanding, and provided a basis for identifying key persons in Mongolia.

3. Data sources

Methods used for searching paper and electronic records, and for interviewing key persons, are described below.

Systematic literature review

Libraries

Searching electronic catalogues of libraries in London¹⁴ for the term “Mongolia” and such as “brucellosis”, “agriculture”, “development”, “economies”, “health”, “governance”, “policy”, “livestock”, “transition” “policy” provided good background information. Besides books, various reports were provided from World Bank, IMF, TACIS Technical Dissemination Project, Asian Development Bank,

¹¹ Economic analysis of the brucellosis control in Mongolia (*Roth F. et al, 2001*)

¹² Dr. Otorino Cosivi was responsible project leader for brucellosis control in the Department for Communicable Disease, Surveillance and Response at WHO Headquarter.

¹³ Dr. Jan Kolar, retired WHO-expert living in Prague, worked for WHO for about 10 years in Mongolia from 1965 onwards.

¹⁴ Consortium of Higher Education Libraries (M25 Consortium London)

UNESCO, and United Nations Centre for Regional Development. The search for “Brucellosis” covered the relevant scientific literature.

Regular search on the web

Web searches concerning “Mongolia” and “Brucellosis” have been conducted throughout to ensure information was up to date. Catalogues of scientific papers such as Pub med, Medline, Web of Science, SIGLE, IBSS¹⁵ and BIDS¹⁶ have been consulted. The catalogues of international organisations, WHO, FAO and O.I.E., were very important. References and citation searches have been applied to the papers identified. This provided comprehensive and up to date information used in chapter 2 on the worldwide epidemiology of brucellosis, on the experiences with applied brucellosis surveillance policies and on the current discussion about this disease.

The observation period of this thesis includes the transition, from a centrally planned country to market oriented economy in the 1990s. Strong impact of such economic transitions on public health have been documented for China, Russia, Eastern and Middle Europe countries, and Central Asian countries (*Adeyi, O. et al, 1997*). Therefore, to consider this in the policy analysis, special consideration was given to the search of publications related to the topic of “Public Health in Mongolia following the transition”.

Processing the information

The relevant publications, books, reports, documents etc. were entered in Reference Manager and filed with a continuous number. This allowed easy physical and electronic access through the search by key words.

¹⁵ International Bibliography of the Social Sciences

¹⁶ Social Science data-base from LSE

Information from Dr. Jan Kolar

Dr. Jan Kolar, retired WHO-expert living in Prague, worked for WHO in Mongolia for about 10 years from 1965 onwards. His task was to elaborate, implement and conduct a brucellosis surveillance strategy for Mongolia. Beside his wealth of experience, which he could communicate as a key person during interviews, he provided reviews, surveys and documents on the policy of brucellosis disease control and epidemiology of brucellosis before the transition. Most of the material provided by Dr. J. Kolar is neither published nor accessible in any archive.

WHO Geneva

Literature identified at WHO headquarter in Geneva

The search for “brucellosis” as well as for “Mongolia” within the WHO-Intranet at the headquarter in Geneva yielded electronic versions of working groups and committees reports, as well as minutes from joint FAO/WHO expert meetings and mission reports. This document search gave a comprehensive overview of the involvement of WHO in the fight against brucellosis in various parts of the world.

In the archive of the WHO library the search within the card index boxes gave references to historical documents not available electronically. The material documented the involvement of the WHO in brucellosis control in Mongolia in the 1960s and 1970s and addressed the first aim (epidemiological patterns) and the second aim (applied surveillance strategy). Most of these documents were assignment reports, mission reports and reviews, in other words internal or unpublished work, so-called “grey literature”.

Dr. Ottorino Cosivi

Dr. O. Cosovi, project leader for brucellosis control in the Department of Communicable Disease, Surveillance and Response at WHO Headquarter, made available his

files related to world-wide brucellosis control which contained relevant documents, such as memorandum, guidelines and notes from conferences or forums.

Mongolia

The data sources presented did not provide all the required information. In order to close this gap, fieldwork was conducted in Mongolia in 2003. The aim of this field work was to get coherent information for the 1966 to 2002 time period for: (i) Aimag level prevalence of brucellosis in sheep, goats and cattle and the incidence of brucellosis for humans; (ii) numbers of produced doses of vaccines Rev.1 and S-19 and data concerning the vaccination process; (iii) information on the different strategies and applied policies in fighting brucellosis in animal and human, including issues concerning governance, share of responsibility, process and results. This was obtained through intensive searching of archives and interviewing key persons.

Archive work in Mongolia

Data on the prevalence of brucellosis in animals was obtained from authorities within the Ministry of Agriculture (MoA) and the Statistical Department. Data on human brucellosis incidence was extracted from authorities within the Ministry of Health (MoH) and the Statistical Department.

Quantitative and qualitative data was used to provide an overview of surveillance policies. The qualitative data was backed up by quantitative data, such as data on testing and vaccination collected from authorities within the MoA. Two different methods were used to collect qualitative data: (i) documentary approach by reviewing published and unpublished literature, local reports, surveys, and government papers in the MoA, MoH, WHO local office in Ulaanbaatar, central Governmental archives, Medical University of Ulaanbaatar and by approaching key informants; (ii) interviewing key personnel, and visiting key sites such as hospitals, laboratories, vaccine production.

Interview with key persons in Mongolia

The contacts with Mongolian authorities (MoH, MoA) and with the local WHO office in Ulaanbaatar, established during previous work ¹⁷, were used for further identification of key persons. Formal interviews with 18 key persons, responsible for brucellosis surveillance at different levels, provided information about the surveillance policy over the time periods. The *appendix 3.1.* lists the interviewees. They could also often provide hints about further sources of documents and data.

4. Methodology used to obtain information during field work in Mongolia

Research partnership

The field work in Mongolia was embedded within a research partnership, that facilitated approaching institutions and coping with the language barrier.

Collaboration, organisation and setting

As first part of this “University Exchange”, Dr. M. Nansalma was a “guest researcher” at the STI in Basel/Switzerland for two months in summer 2003. Her focus was a scientific exchange with the research group “Human and Animal Health” on epidemiology and health policy. She was there for specific training to develop statistical methods and tools.

As second part of this “University Exchange”, the author carried out field work as a “guest researcher” at the MAS in Ulaanbaatar/Mongolia for one month, in autumn

¹⁷ The author conducted in 2000 an economic analysis of the whole herd vaccination programme (Roth F. et al, 2001). This network amongst Mongolian policy makers and scientists could be completed at the occasion of the presentation of this analysis at the Second National Workshop on Brucellosis Control in Ulaanbaatar in 2001.

2003. The field work in Mongolia served to establish further contacts with concerned authorities and scientific experts in order to complete gaps of information and data. Key persons were interviewed and unpublished material tracked down.

Participation

The collaboration with M. Nansalmaa was crucial for many types of data collection during the field work. With her participation, archives could be accessed in Ulaanbaatar and searched for reports, government documentation, data as well as all related unpublished scientific material. As all scientific documents were in Russian, and all policy papers were in Mongolian, she translated them into English, after having traced and discussed with me which parts were relevant for the research questions.

Her broad network helped identifying further of key persons for interviews to fill information gaps. She also provided valuable support in establishing contacts with local authorities in Khuvsgol Aimag, where additional field work was conducted. M. Nansalmaa also acted as interpreter since the key persons interviewed in Mongolia were all non English speaking Mongolians.

Interviews with key persons

Selection of interview partners and interview sites

M. Nansalmaa complemented existing contacts within the authorities from her own network within the Mongolian Health System, and her knowledge of the organisation of the authorities at different levels. The candidates for the interviews were selected jointly with M. Nansalmaa to include: Key persons from all the authorities responsible for the control of brucellosis in animals or in humans at three administrative levels: central level, Aimag level, and Soum level, and patients ill from brucellosis were interviewed. Further interviews took place with herder families and scientific experts on brucellosis. This selection of interview partners provided a view

of the policy and actions taken concerning brucellosis control and treatment, from the perspective of the different groups.

For the interviews on the level of Aimag and Soum, the Aimag of “Khuvsgul” in the northern part of Mongolia along the Russian border was chosen. The choice was logistical, as M. Nansalma had worked there for 16 years¹⁸, and her broad network facilitated contacts with key persons.

Khuvsgul Aimag has a surface of 100,600 km² and a total population of 121,000 (2002). The population density (1.21 person/km²) is slightly lower than the national average (1.58 person/km²). The prevalence of brucellosis was at 0.4% for sheep and 1.1% for cattle (all data are means for 2000 to 2002), close to the Mongolian average (0.5% for sheep and 1.1% for cattle). However, the data for the incidence of brucellosis in humans differ between Khuvsgul Aimag (0.75 / 10,000 inhabitant) and the whole country (7.5 / 10,000). As we had noticed during the interviews with key persons from the Aimag Hospital in Moron, the reason for this was lack of test kits for serological diagnosis in this Aimag rather than the successful prevention of infection in humans.

Interview technique

The interviews were semi-structured. The questions were prepared in advance to meet the specific aim of the single interview. But depending on the circumstances and preferences of the interview partners, the single interviews were finally conducted in a structured, semi structured or open way. A brief description of the topic of interest had been given when arranging the appointment. Most interview partners were therefore prepared for the interview and sometimes even had some written material to show or to give.

¹⁸ She worked first as physician, then as director and state senior inspector in sanitation and epidemiology.

Most interview partners were visited at work; two elder interview partners were pensioned and came to see us in the offices of the Mongolian Academy of Sciences. Most interviews lasted between one and two hours and were often followed by a visit of the site, lunch or tea. Thus, the overall time of contact leading to further discussion was considerable.

Documents and data search

Organisation of the search

The document and data search in Mongolia was based in Ulaanbaatar for practical reasons. Material from local Aimags was only included if reported to the Central Government in Ulaanbaatar. There are some decentralised archives in various Departments and Ministries such as the Central Governmental archive, archive of the Veterinary Laboratory, archive of the Statistical Department, archive of MoH or archive of the Biocombinat¹⁹. But it turned out that most of these archives had material on policy filed only from 1991 onwards. After 1989 the country had shifted from a socialist state to a democracy and from a centralised to a market economy. In 1992, a new constitution was adopted based on democratic principles. Thus, for our field work, informal pathways were set up to search materials related to policy prior to 1992.

As international Organisations have been involved in brucellosis control in Mongolia since the early stages of the fight against this disease, the local offices of UNDP and WHO were included in the archive search. UNDP keeps files for 7 years concerning financial matters, and 5 years concerning technical issues. There was no relevant technical report in the UN house library, and the archives of the WHO local office were not organised in a way that facilitated searching. As a result, WHO documentation is restricted to what could be found in the office rooms of WHO.

¹⁹ Plant in Songino, close to Ulaanbaatar, to produce vaccines against Brucellosis

Searches in the catalogues of the Medical University of Mongolia allowed access to all scientific work on the epidemiology of brucellosis in Mongolia, including research carried on before “transition”.

Procedure in finding policy and scientific documents and data

Policy and scientific documents

As stated above, generally, policy papers concerning the period prior to democratisation could not be found in archives. So other informal ways had to be used to find them.

In order to locate them, knowledge of the existence and identification of every single policy paper was needed. Some of our older interviewees could show us one or two governmental documents such as “Government Resolution” or “Order of the Ministry”. The number and date of the previous documents, which had to be replaced, were often mentioned in these documents. Reports referring on existing Governmental papers gave further hints about their existence. But still, they mostly had to be found in someone’s office or maybe in the local archive of a department. Documents had to be found in an informal way, which meant through older key persons or somebody knowing key persons having these documents.

Out of the interviews and document search a list with 24 Governmental papers on policy and strategy for fighting brucellosis, covering the time frame between 1959 and 2003 was compiled. Some of them we already had found and were crucial as starting points for further searches. Others, we only knew of their existence, or assumed that they must have existed in order to fill the policy gap supposing brucellosis control was continuous.

A second list of 12 items of scientific papers on brucellosis was compiled from hints from key persons and catalogues from the Medical University in Ulaanbaatar.

Some policy and scientific papers were identified during fieldwork. After fieldwork, M. Nansalma found the missing documents and translated them. She translated all documents but seven. These were translated by a colleague (Oyunaa Tsedendorj). As some scientific papers were long, only extracts were selected for translation.

Human data

The data concerning the spread of brucellosis in humans was found from: (i) officially published data from the MoH, or the State Statistical Office of Mongolia (SSOM), and (ii) from unofficial data mostly relating to data collected by the Infectious Disease Research Institute (IDRI).

The official data from the MoH were published in various papers such as “80 years Health Sector of Mongolia” (*Bayart B. et al, 2001*), “Health Statistical Report 2002” (*The Directorate of Medical Services, 2002b*), “Health Indicators 2002” (*The Directorate of Medical Services, 2002a*), “Health Statistical Data in 1960 - 2002” (*Health Development Centre, Mongolia, 2002*), “State Hygiene and Epidemiological Statistics Data (1952 – 1997)” (*State Statistical Office of Mongolia, 2000*), and “Health Statistics of Mongolia 1960-1992” (*Ministry of Health et al, 1993*).

There are two main problems with the officially published data: (i) the MoH, or SSOM data include only reports from the Aimags to the capital (MoH), and variations may have occurred in case definition (clinical diagnosed, serologically confirmed), in the reliability of reporting to the capital, and in the governance in the Aimags. (ii) The available datasets are not continuous for all Aimags from 1966 to 2002. For the time period before 1993, there are missing data at Aimag level, and before 1980, there are nearly no continuous data available from the MoH, or SSOM, except a figure for “Brucellosis incidence 1958-2000” at national but not Aimag level (*Bayart B. et al, 2001*).

The data gaps were filled mainly through the IDRI. This Institute has systematically collected data on brucellosis since 1966, but these data are not officially published and generally show a higher incidence (*The Directorate of Medical Services, 2002b*)

(*Infectious Disease Research Institute, 2004*) (*Honhold N., 1995*). These data result from surveys, and systematic investigations with the involvement of researchers of the IDRI (*Infectious Disease Research Institute, 2004*), or even particular studies carried out in one or two Aimags per year, in which people from high risk groups were selectively sampled (*Honhold N., 1995*).

Therefore the human data obtained of this research may result from a mixture of collection methods, of case definitions, and of sampling methods. This was considered when carrying out the analysis.

The human population was taken from data provided by the Infectious Disease Research Institute (*Infectious Disease Research Institute, 2004*) for early years up to 1990 and from officially published sources afterwards (*State Statistical Office of Mongolia, 2000*) (*State Statistical Office of Mongolia, 1994*) (*State Statistical Office of Mongolia, 1999*) (*National Statistical Office of Mongolia, 2003*) (*Mongolian Statistical Office, 2004*). All sources seemed to correspond to each other where there was an overlap of reported data, thus these data appear to be consistent.

Animal data

The sources of animal data were not as varied as for human data. Official statistics provided the data on animal population (*State Statistical Office of Mongolia, 1974*) (*State Statistical Office of Mongolia, 1996*) (*State Statistical Office of Mongolia, 1999*) (*National Statistical Office of Mongolia, 2003*). One main source provided data on the sample size of tested animals (cattle, sheep and goat) and the corresponding cases with brucellosis (*Ministry of Agriculture, 2003c*). These statistics were unpublished. The dataset was largely complete. As these data have been compiled by one single entity (Central Veterinary Laboratory of the Ministry of Food and Agriculture), the consistency concerning case definition and methods of compiling the data are more reliable. However, uncertainty remained as to how the sample for testing the animals was designed. The other uncertainty related to how many herds were used. As described in chapter 2, the compilation by herd or area is important for considering the epidemiology of brucellosis.

Surveillance data

The data concerning the planning and implementation of the vaccination in animals was obtained through an intensive archival search at the State Veterinary & Animal Breeding Department of the MoA. This department was responsible for implementing the vaccination campaign against brucellosis in Mongolia. The data however were not assembled and had to be collected from yearly files reported in different formats.

The data concerning the production of the Rev.1 vaccines have been used for verifying and crosschecking the plausibility of the data on vaccination implementation. They were obtained through archive search at the Biocombinat factory located in Songino-Mongolia²⁰ (pers. Communication with ULZIITOGTOKH Tsedev, Vice-Director, 2.10.2003 (*Roth F., 2003a*)). All Rev.1 vaccines used for the vaccination campaigns since mid 1970s had been produced at this factory. Data on the production of S-19 vaccines were only available for the years after 1996. Before then cattle were also vaccinated with Rev.1. All these primary data found in archives were drawn out of internal reports or production files. As they were in Mongolian, the archive search was conducted by a staff member according to our requirements.

Recapitulation on obtaining information

To recapitulate this section on data collection methodology, most of the documents and data uncovered during the Mongolia field work were unpublished, sometimes in the form of handwritten notes. Tracking down Governmental policy papers about brucellosis control turned out to be rich in impediments: they were not incorporated into a single archive, but were disseminated among various archives of the different authorities, within the MoA and MoH, and the Central Government Archive (CGA). As the access to this CGA was restricted to authorised persons, the research partner-

²⁰ This state-owned factory produces over 60 types of bio preparations and aims to satisfy 100 percent of the domestic market.

ship established with M. Nansalmaa and the MAS helped. Still, most of the governmental decision papers could only be obtained from key informants who had put their own copy at our disposal. M. Nansalmaa played a key role in establishing contacts in Ulaanbaatar, accessing archives, tracking down the documents and translating them into English.

5. Quality assurance

Data cleaning

The collected data documented the prevalence in animals (sheep, goats, cattle) and the incidence in humans, at the Aimag level, for the period 1966 to 2002. This resulted in about 17,000²¹ single items entered in *Access* to form unique and comprehensive database.

For data cleaning, the database was transferred to *Excel* and *Intercooled Stata* using *Stat Transfer*. This allowed for eliminating of mistakes made in data entry (checking) and to assure the reliability and validity²² of the primary data. Crosschecks with plausibility calculations in *Excel* were done, such as calculation of prevalence, incidence and totals. Plots of the data with *Intercooled Stata* were made to show any unusual constellations caused by mistakes in data or data entry. If mistakes were identified the original data were checked for inconsistencies.

The original data sources were cross-checked with other data sets or overlapping data sets. For example, the production of vaccines was checked with the implemented vaccine programme, and with the planned vaccination programme. The inci-

²¹ Collected data for animals (cattle, sheep, goats) for every Aimag and all years (1966 to 2002): totals in population, samples, positives, prevalence, vaccinated (planned, effective, with Rev.1 or with S19 vaccines). Collected data for humans for every Aimag and all years: population, number of new cases, incidence. Collected data on vaccine production: for Rev.1 and S19 during the observation period at central level.

²² Reliability & validity: “the two key concepts that determine the accuracy of surveillance data are reliability and validity. Reliability refers to whether a particular condition is reported consistently by different observers, whereas validity refers to whether the condition as reported reflects the true condition as it occurs.” (Teusch Steven M. et al, 2000)

dence of brucellosis at national level had been calculated with the total Mongolian population as the denominator, however, for some Aimags the numerator was missing for the period between 1979 and 1990 and could have caused published incidence rates to be too low (*Bayart B. et al, 2001*). It appeared that “zero” and “missing” were not distinguished. This was adjusted: the denominators representing the total Mongolian population have been diminished by the population of the Aimags with missing values (numerator). The aggregation used in the spatial analysis was not correctly weighted by the number of animals per Aimag to derive the number of cases. Instead, the aggregation was based on the samples of positive cases irrespective of population in the Aimag. This was corrected.

Quality assurance of grey literature

Grey literatures provided a rich source of information and often gave indications about important discussions, controversial views or trends. However, this grey literature did not undergo any scientific peer review. Numbers, implemented policies, and technical details included in this thesis work have been checked and verified by triangulation with other information such as published literature, confronting interview partners, or comparisons with other documents not quoting each other. Through this procedure, potential bias was minimised.

Quality assurance of interview

M. Nansalmaaa acted as interpreter. Quality assurance of the translations was done through asking the same question differently when the question was crucial, or the answer given doubtful. This led several times to further discussions, where the answers were refined or even changed. This was not always because of translation problems, the interviewee sometimes revised his or her opinion. Numbers mentioned during the interview were written down and shown to the interviewee. When appropriate, sketches were drawn and developed during the follow up talks and the state

of knowledge shown on a graphic illustration. So during discussion the information gained in the interviews could be backed-up, qualified or rejected, which improved the quality of the content. Because of consecutive translations, there was enough time for taking notes about the conversations. After the interview, all notes were written down in a standard format and were discussed and revised with M. Nansalmaa. Missing or unclear information could be revised, sometimes by contacting interviewee. This process of triangulation was continued by comparing or completing the interview-information with official documents on brucellosis control.

Quality assurance of translations

M. Nansalmaa scanned and sent the original documents together with her translations by E-Mail. To assure quality, she worked through the translation with other English speaking persons living in Mongolia. The purpose of this quality control was to check the English and not correct the translation, as these persons were not all experts in the Mongolian or Russian languages.

Working through these translations and having the originals allowed some plausibility control, for example, with numbers and tables, but also by cross-checking the coherency of the content. Questions and comments were sent back to M. Nansalmaa. No doubt some weaknesses in interpretation remained, but this process provided documentary evidence of good quality and reliability.

6. Analysis

Plotting and mapping the data

Various graphs have been created to get a first overview on the data. Graphs showing the spread of disease are included in chapter 4; graphs showing surveillance policy and the course of disease are included in the chapter 5; comprehensive set of

graphs with human incidence and animal prevalence in every Aimag are in the *appendix 4.2.*

The data have been mapped with a geographical information system (GIS, *MapInfo software*) to get a view of the spatial distribution of brucellosis. Maps showing the population density of humans and animal as well as the spread of disease are included in chapter 6. Comprehensive sets with the incidence in humans, together with the prevalence in SR, and with immunisation process, are in *appendixes 4.1. and 5.1.* As there is one map per year, the dynamic infection and recovery process over the whole observation period 1966 to 2002 are shown in short consecutive time slots, in the manner of a film presentation. The template map of Mongolia has been downloaded from internet²³.

The illustrations of the worldwide spread of *B. melitensis* and *B. abortus* (*see chapter 2*) have been given on maps processed with *MapInfo*. The template map has been downloaded from internet²⁴.

These graphs and maps provide the first overview of this collection of new data and establish the basis for the first qualitative and quantitative analysis to be carried out using it.

Analysing the surveillance policy

To assess the surveillance policy of the Mongolian authorities, a qualitative analysis has been performed (*see appendix 6.1.*). A framework defining the basic elements of best practice in disease surveillance has been elaborated, based on literature concerning disease, and more specific, brucellosis surveillance (*see chapter 6.1.*). This

²³ <http://www.cipotato.org/DIVA/data/DataServer.htm>

²⁴ <http://www.rbgekew.org.uk/gis/tdwg/index.html>

framework was applied to assess the surveillance policy of the Mongolian authorities.

The first step of the analysis was to sort out the policy papers in chronological order. Missing papers could be identified as they were usually mentioned in the ensuing papers replacing them. The missing documents have been searched for according to the procedures described earlier.

The second step was to identify the methods for *control*, *eradication* or *prevention*, as foreseen in the policy papers. The available methods for brucellosis surveillance are: “*test and slaughter*” of seropositive animals (T&S), “*vaccination*” of animals, and the application of “*hygiene methods*” or “*management practices*” (see chapter 2). The methods planned by every single policy paper have been analysed. “*Education campaigns*” initially played an important role in the policy to preventing brucellosis in Mongolia, and they were listed as a separate method item, although this is not really a separate method, but rather serves to reinforce other methods, such as implementing *hygiene methods* or *management practice*.

In the third step, analyses of the policy papers have been entered into a grid containing the basic elements of surveillance. This gold standard required the following elements: (i) definition of objectives; (ii) case definitions; (iii) data collections; (iv) data analysis; (v) dissemination; (vi) implementation; and (vi) evaluation (see chapter 6.1.). As a result, the strength and weaknesses of the policy was evaluated. This allowed potential gaps in the Mongolian brucellosis surveillance system to be identified, leading to further analysis.

Mathematical and statistical analysis

Mathematical and statistical methods were applied to meet the third aim, which was the analysis of possible interactions between the surveillance strategies applied and the spread of disease.

To capture the transmission between animal the *Kermack-McKenrick Susceptible Infectious Recovered Model* (short: *SIR model*) has been used. This epidemiological model computes host/parasite population dynamics over time, for a generalised contagious illness, in a closed population (*Kermack O W et al, 1927*). This model involves coupled equations with no unique solution, relating the numbers of individuals in the following three compartments: *Susceptible*, *Infectious*, and *Recovered*. Mathematical modelling process fitted the deterministic equations and gave estimates of the baseline birth and mortality rates, as well as on the transmission coefficient. For this mathematical modelling the *Ventana Simulation Environment Vensim*, a system-analysis software was used.

Statistical regression analysis has been used to identify the dependency of the infection in humans on animals. To distinguish the infection source among the different kinds of animals, and to identify potential cofounders, use was made of multiple regression with both covariates cattle and SR. The *Stata* software was used for these analyses.

This section described the methodology applied for the qualitative and quantitative analysis. Descriptive methods were used to grasp the spread of disease over space and time (aim 1). Qualitative analysis was used to assess the surveillance policy (aim 2). Both provided the basis for further mathematical and statistical analysis, assessing the underlying interactions between the surveillance strategies and the spread of brucellosis (aim 3). From the results of the analysis, conclusions for further policy implications were drawn producing the final key output (aim 4). For this, results and implications of all three previous aims have been triangulated and combined, allowing the formulation of appropriate recommendations for further improvement in surveillance policy.

Epidemiology of Brucellosis in Mongolia

Chapter 2 has provided the basis necessary for understanding the complex features of the zoonosis brucellosis, and placed Mongolia in the international context. The comparative analysis of the spread in SR and humans between Mongolia and the Near East Region, one of the most contaminated regions of the world, has shown that Mongolia has a relative low prevalence in animals and a high incidence in humans. The speculation of this epidemiological facet was that it was due to the close animal - human contact, which might be encountered in a nomadic setting found in Mongolia.

This chapter is dedicated to the first aim of this thesis, which is: *“to establish epidemiological patterns of brucellosis in animals and humans in Mongolia from 1966 to 2002.”* The fulfilment of this first aim gives a basis from which to tackle the second aim: *“to provide an historical overview on the different strategies applied to the control of brucellosis in Mongolia”*. This will be treated in chapter 5.

The empirical evidence on the spread of brucellosis in Mongolia was gained through intensive data collection, described in chapter 3, from diverse Mongolian authorities and archives in Ulaanbaatar. The collected data have been assembled in a unique and comprehensive database, covering the prevalence in animals (sheep, goats, and cattle) and the incidence in humans, on the basis of each Aimag, for the period 1966 to 2002.

The scientific evidence on the epidemiological patterns of brucellosis in Mongolia has been drawn from various sources, described in chapter 3:

(i) Key persons, who had past or current involvement in policy or its application, have been interviewed²⁵. Besides members of the Mongolian authorities and Mongo-

²⁵ The list of all interviewed persons in Mongolia is given in the *appendix 3.1*.

lian scientists, Dr. Jan Kolar was a central source of information. His observations about the etiology of brucellosis have been considered in the second section of this chapter;

(ii) Reports in English about brucellosis control in Mongolia.

(iii) Little scientific work on brucellosis in Mongolia has been published so far in peer reviewed journals in the English language. However there was some scientific literature about brucellosis in Mongolia written in Mongolian or Russian and which has been tracked down by intensive search in Ulaanbaatar.

This chapter begins with an account of the history and evolution of brucellosis in Mongolia. It provides the empirical and scientific evidence on the spread of brucellosis. Comprehensive epidemiological studies had started in the 1960s, though the origin for this laid in the 1950s with the arising awareness of the problems caused by brucellosis. The epidemic situation described in this section were closely linked to the control policies and provided evidence for defining them. As the central research question of this thesis was to determine whether there was a relationship between the stated surveillance policy and the brucellosis prevalence in animals and the brucellosis incidence in humans, it was necessary to consider first the spread of disease and then the control of disease.

In the second section of this chapter the etiological aspects of brucellosis in Mongolia have been elaborated. In chapter 2 we have seen that adapted management practices were crucial for preventing the transmission of brucellosis between animals, and that there were mainly two routes of brucellosis transmission from animal to human: the food borne transmission with unpasteurised infected milk and its products, and the infection related to occupational hazard, such as respiration, cutaneous contact, conjunctival contact or auto-inoculation. Therefore the management practices actually applied in Mongolian have been assessed in order to understand their role in spreading disease and the scientific literature exploited and the significant routes and modes of transmission relevant for the Mongolian context analysed. This section has provided important knowledge for assessing the brucellosis control policies and considering whether the measures taken effectively met the etiology.

In the last section of this chapter the limitations of this epidemiological analysis have been elaborated and discussed. Though this chapter could meet the first aim of the thesis – it provided a broad and comprehensive knowledge on the epidemiological pattern of brucellosis in Mongolia, based on empirical and scientific evidence - there still remain some limitations. These concerned the identification of infection by individual animal rather than by herd and data quality.

1. History and evolution

Early case records and development before 1963

With the assistance of the Soviet Union veterinary specialists conducted brucellosis surveys in Mongolia in 1924 and again in 1926 and they did not find any evidence for brucellosis (*Enkhbaatar L et al, 2004*). But in 1932, the first case of brucellosis was detected in cattle in Selenge Aimag (*Dashdavaa J, 1969*) (*Damdinsuren L, 1972*). In the early 1940s, abortions in sheep and cattle occurred frequently in several farms, and brucellosis was confirmed by lab tests (*Enkhbaatar L et al, 2004*) (*Damdinsuren L, 1972*) (*Baldanderj T, 1972*). Eventually, in 1949, the first case of human brucellosis was officially registered (*Enkhbaatar L et al, 2004*).

In 1950, the level of brucellosis infection was 17% in cattle, 3.5% in sheep and 2.02% in goats (*Enkhbaatar L et al, 2004*). Since then studies on brucellosis have been implemented on a regular basis showing a continual high prevalence in animals (*Dashdavaa J, 1969*). Out of 700 samples taken from animals in the slaughterhouses in Ulaanbaatar (UB) in 1959, 10% to 20% were sero-positive (*Roth F., 2003b*).

However, only a few patients were treated during the 1950s for brucellosis²⁶. The brucellosis incidence in humans was reported between 4 and 17.8 per 10,000 inhabitants throughout Mongolia during the 1950s (*Baldanderj T, 1972*). Surveys among

²⁶ In the Hospital for Infectious Diseases in UB from 3 patients in 1953 to 42 patients in 1957 (*Enkhbaatar L et al, 2004*).

risk groups such as farm and slaughterhouse workers, or veterinary specialists showed the following dramatic infection' rates, using skin allergy tests (Burne and Huddleson): 1953: 24.5% to 37.3% (*Dashdavaa J, 1969*); 1956: 31.4%; 1957: 20% to 30%, 1956/57: 13.4% and 1958/59: 36.8%. As more than 70% of the population was working in the livestock sector (*Enkhbaatar L et al, 2004*) and 40% of the population had contact with animals (*Dashdavaa J, 1969*), this situation was alarming and led to a Resolution of the Ministers' Cabinet in 1959 (*Molomjamts et al, 1959*) to investigate further the epidemiology of brucellosis in cattle (*Damdinsuren L, 1972*). Workers in factories processing animal products such as textiles and meat were threatened as well as the rural population.

Epidemiological studies 1963 to 1968

The proper attention to brucellosis was given when it became a serious human health problem. The Mongolian Government turned for assistance to WHO and the COMECON States.

WHO project Mongolia 0001 on "Strengthening of Health Services (Epidemiology)"

The Mongolian People Republic (MPR) had become a member State of the UN in 1962. Little was known about the health status of the population. A WHO epidemiological team initiated a study of the country's epidemiological problems with a view to instituting control measures the same year. The public health problems appeared to be mainly concerned with infectious diseases, spread all over the country (*Jezek Z. et al, 1969*). With the industrialisation, potential for meeting people increased. Thus the modernisation of life styles favoured the spread of infectious diseases.

A year later, the Mongolian Government launched an epidemiological analysis of infectious diseases with the assistance of WHO (Resolution of the Minister's Cabi-

net Nr. 52 on 14.02.1963) (*Enkhbaatar L et al, 2004*). That same year the WHO project Mongolia 0001 on “Strengthening of Health Services (Epidemiology)” started as a long-term project to (*Jezek Z., 1970*):

- (1) Undertake special epidemiological surveys of the prevailing communicable diseases to determine their nature and extent;
- (2) Draw up a programme of priorities for effective prevention and control measures.

As available routine morbidity data was of little value -- due to diagnostic difficulties, inadequate laboratory facilities and reporting failures -- multi-subject immunological surveys were performed. The purpose was to identify antibodies of the human population and of farm animals, and grasp the epidemiological situation to elaborate an epidemiological surveillance system.

Epizootiological studies

In 1963 – 1965, epidemiological teams headed by WHO experts, carried out wide scale brucellosis studies in animals (*Damdinsuren L, 1972*). The objectives were:

- (i) To assess the prevalence of brucellosis in livestock, as a necessary support to epidemiological investigations of brucellosis in humans.
- (ii) To explore the specific local factors arising from natural conditions and existing animal husbandry practices favouring the spread of brucellosis among livestock.
- (iii) To organise and carry out controlled field trials of *B. melitensis* Rev.1 vaccine on small ruminants, and to assess its preventive value in immunising Mongolian livestock (*Cvjetanovic V. et al, 1968*).

They investigated the prevalence of brucellosis on a flock basis to assess disease occurrence and distribution and derive adapted control strategies, as it is essential in brucellosis surveillance to consider the flock or herd as the primary epidemiological unit, and to estimate its prevalence (as opposed to individual prevalence) (*Food and Agriculture Organisation of the United Nations Rome, Italy, 1992*). Because of the possibility of latent or dormant brucellosis infection, the entire flock should be re-

garded as infected, even if only one animal proves to be positive (*see chapter 2*). Sheep and goats were treated as one group (small ruminants, or SR) as they were raised together in common flocks usually with a sheep/goats ratio 3:1 or 4:1 (*Cvjetanovic V. et al, 1968*). The study included 680 randomly selected flocks, consisting in 413 SR' flocks, 92 cattle flocks, 89 camels flocks and 86 horses flocks with a total of 16,479 animals in 6 Aimags²⁷ (*Cvjetanovic V. et al, 1968*). The collected samples were examined with SAT and CFT. Interpretation of SAT was done in accordance with recommendation of the Joint FAO/WHO Expert Committee on brucellosis (Fourth Report) (*Cvjetanovic V. et al, 1968*). This ensured an international standard and an international unitage system. Flock infection rates were 43.0% for cattle, 16.2% for sheep, 13.4% for goats, 4.9 % for camels and 30.9% for horses (*Damdinsuren L, 1972*). Although, sheep and goats were kept together in common flocks and formed one epidemiological unit, infection rates were often given separately.

This epizootiological survey by the WHO assisted team provided the basis for the planning of control strategies. However, the seriousness of the situation prompted the MoA not to wait until the WHO assisted project had elaborated a control strategy. The MoA started the following year a separate action assisted by the COMECON States and directed toward control of animal brucellosis by T&S method (*Kolar J., 1995b*).

Brucellosis serological survey in humans

Although brucellosis was, as outlined above, first reported in 1932, it was difficult to assess the incidence and prevalence because of the immense number of very mild and therefore undiagnosed cases. The only reliable estimates were serological tests in populations sampled at random, carried out by the WHO epidemiological team. The survey was carried out during November 1966 – November 1967, during which the serum of 4,816 persons were simultaneous tested with SAT and CFT (*Jezek Z., 1970*). The tests covered 0.5% of the Mongolian population.

²⁷ Central Aimag, Bulgan, Zavkhan, Uvurhangai, South Gobi, Dornod

In urban population, 1.7 % of the persons tested were serum-positive, whereas in rural population there were 4.4 % serum-positives. There were significant differences among the different Aimags and Soums examined for this survey, which varied from 0.6% to 9.6% (*Jezek Z., 1970*). It was also found that the percentage of human reactors depended on the occurrence of brucellosis in farm animals, particularly among sheep (*Jezek Z., 1970*). The infection rate with brucellosis was as follows: (i) in urban areas: 13.7% among meat workers, 2.3% for dairy workers, 2.1% for students employed in the Agricultural Institute; and (ii) in rural areas: 9.9% in shepherds, 8.4% among farmers, and 3% in non-agricultural work (*Jezek Z., 1970*).

Brucellosis was confirmed as a serious public health problem, and it seemed worthwhile to undertake a third study on special patterns of *Brucella* infection in human and farm animals (*Jezek Z., 1970*). These results ²⁸ reconfirmed the grave influence brucellosis had on public health: nearly all the population living in endemic areas were under permanent risk of *Brucella* infection (*Jezek Z. et al, 1969*).

Test and Slaughter campaign with COMECON assistance

During the WHO project -- independently from the planned elaboration of control strategies based on the surveys-- the MoA launched with the assistance of COMECON States a large Test and Slaughter (T&S) national campaign from 1966 to 1968. The COMECON provided about 30 veterinary diagnostic teams equipped with mobile laboratories (*Kolar J., 1995b*)²⁹. In collaboration with the Mongolian veterinary services, they examined 1,523,632 cattle and yak, 7,723,526 sheep, 2,582,398 goats, 191,355 camels, 4,564 pigs, 4,160 dogs and approximately 800 reindeer with allergic skin test and partly with SAT and CFT during the first year (1966) (*Tserendash Choijiljav, 1972*). The identified reactors were immediately separated and slaughtered (*Kolar J., 1995c*).

²⁸ 15.7% of the animal production workers were serum-positive, 14.7% of the plant production workers, and 10.7% of the non-agricultural professions.

²⁹ Other sources report 40 teams (*Kolar J., 1995a*) or 18 detachments with between 84 to 124 sub-groups (*Ariunaa O, 1996*).

The Mongolian Government stated that the results of these examinations confirmed the surveys of the WHO team: (i) brucellosis was widely spread; (ii) brucellosis was unevenly distributed; (iii) the flock infection rate was extremely high (79% in sheep/goat and 87% in cattle) (*Kolar J., 1995b*). However there were no official relations between the COMECON funded project and the WHO funded project institutionalised at that time (*Kolar J., 1970a*), as the authorities were reluctant to present the epidemiological situation to the outside world because of the threat of losing important markets for Mongolian meat and other animal products (*Kolar J., 1972*). Today, no results on the investigations of the COMECON are available.

Epidemic situation and involvement after 1966

The spread of Brucellosis in humans and animals on Aimag level in course of the time

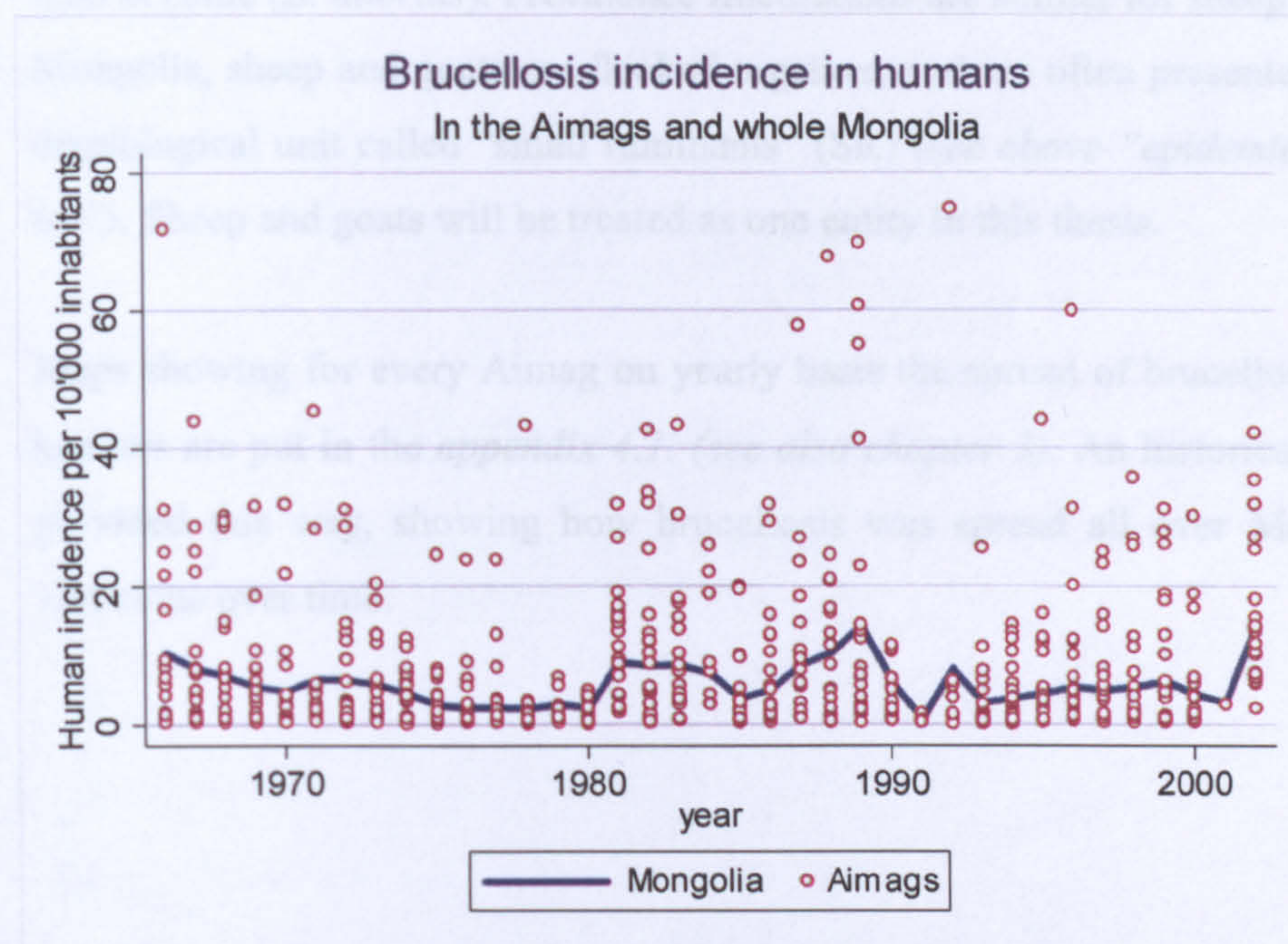
The data were collected during field work in Mongolia in autumn 2003 (*see chapter 3*). A comprehensive database was then generated to describe and analyse, at Aimag level, the spread of brucellosis for the years 1966 to 2002 for sheep, goats, cattle, and humans.

Figure 4.1. shows the incidence of brucellosis in humans, where every dot represents the incidence within an Aimag³⁰. The incidence of every single Aimag has been weighted with its population size to calculate the average incidence of the whole country (=showed as line in the plot). Thus, the yearly incidence of Mongolia varies from 0.67 and 14.33 per 10,000 inhabitants, and has an incidence with an average of around 6 per 10,000. In an international context, this is a high incidence of human brucellosis. The map of the human brucellosis distribution in chapter 2 shows only such high incidences in the Near East Region and the Arabian Peninsula. Nevertheless, the *figure 4.1.* shows that, on average, brucellosis in humans has remained steady, even though trends are noticeable during some decades; in the late 1960s and

³⁰ Two outlying Aimags with incidence over 80/10,000 are not showed in the plot: Gobisumber 2002 inc. 93.6 and Suhbaatar 1990 inc. 85. However in the analysis they are included.

1970s, the incidence declined, but in the 1980s it was volatile and at a higher level, and finally, in the 1990s it rose again.

Figure 4. 1.: Brucellosis incidence in humans



Derived from material collected for this thesis

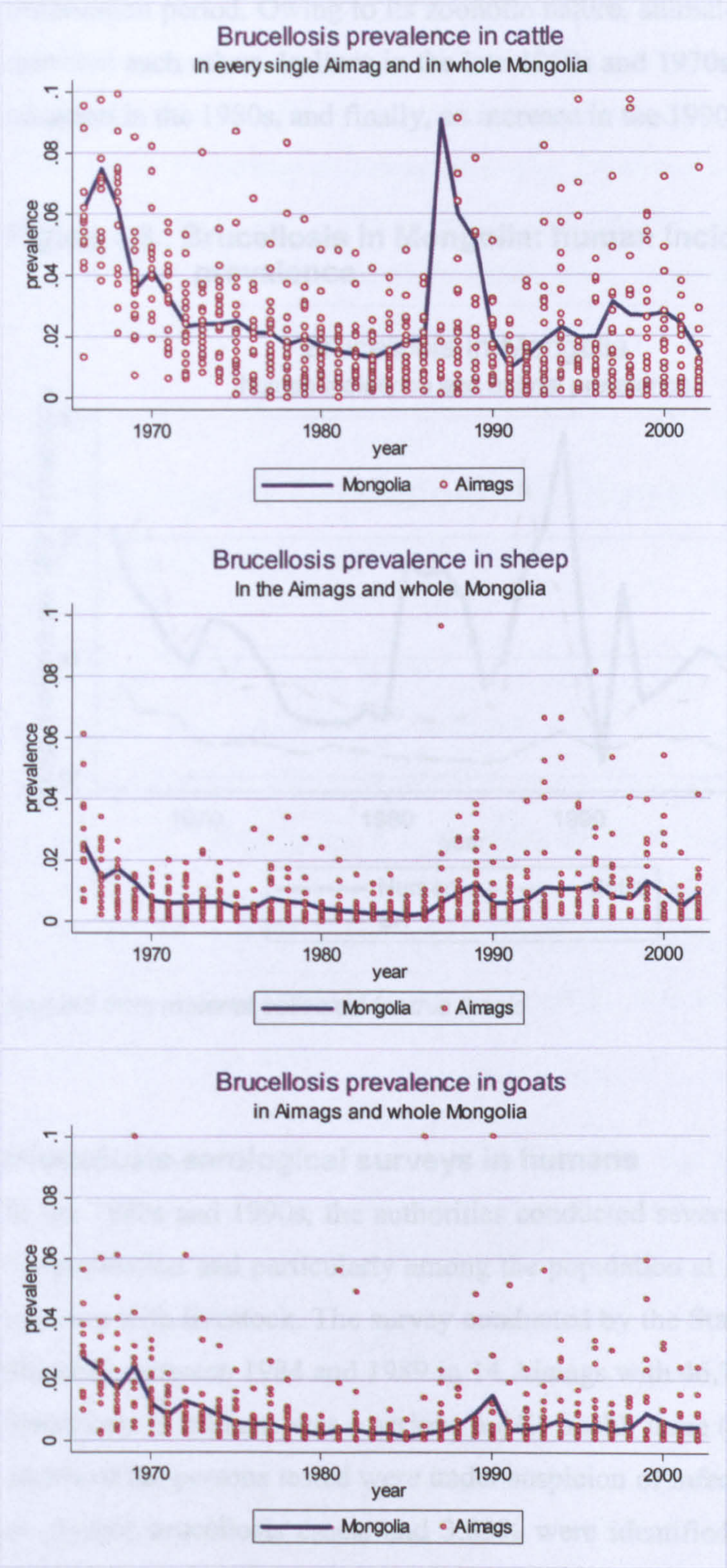
Because the human infection has its origin in the animal disease, the animal prevalence is of great interest. The *figure 4.2.* shows the prevalence in cattle, sheep and goats. As in *figure 4.1.*, every point represents the prevalence within an Aimag³¹, and the average calculation (line) has been weighted with each Aimag's animal population. The prevalence in cattle varies over a broader range than in sheep and goats, and the average prevalence in cattle was much higher. It varied between 0.97% and 9.08% for cattle, with an average of 2.9%, and varied between 0.18% and 2.54% and 0.11% and 2.71% in sheep and goats respectively, with an average of

³¹ The outlying Aimags with prev. over 0.1 are not showed in the plot, but included in the analysis. It concern for cattle in 1987: Arkhangai (0.199), Bulgan (0.12), Dornod (0.20). Selenge (0.16), Tuv (0.15), Khuvsgul (0.16), Hentiy (0.15). It concerns for cattle in 1988: Arkhangai (0.155), Bayanhongor (0.20), Sukhbaatar (0.16). In concerns for cattle in 1989: Bayan-Olgii (0.14), Dundgobi (0.198), Uvs (0.139), Khovd (0.119). For sheep it concerns: Sukhbaatar 1968 (0.168) and Bayankhongor 1969 (0.118). For goats the three outlying Aimags have been set at 0.1 for plotting (not for analysing): Bayankhongor 1969 (0.109), Ulaanbaatar 1986 (0.136), Bayankhongor 1990 (0.105).

0.77% for sheep and 0.75%.for goats. In chapter 2, the worldwide incidence of brucellosis in animals is shown for *B. abortus* and *B. melitensis*, and has been classified as “high” for *B. abortus* and “low” for *B. melitensis* in Mongolia. Thus in an international context, the spread of disease is less important in SR (*B. melitensis*) than in cattle (*B. abortus*). Prevalence fluctuations are similar for sheep and goats. In Mongolia, sheep and goats are flocked together, and are often presented as one epidemiological unit called “small ruminants” (SR) (*see above “epidemiological studies”*). Sheep and goats will be treated as one entity in this thesis.

Maps showing for every Aimag on yearly basis the spread of brucellosis in SR and humans are put in the *appendix 4.1. (see also chapter 3)*. An historical overview is provided this way, showing how brucellosis was spread all over Mongolia, with variations over time.

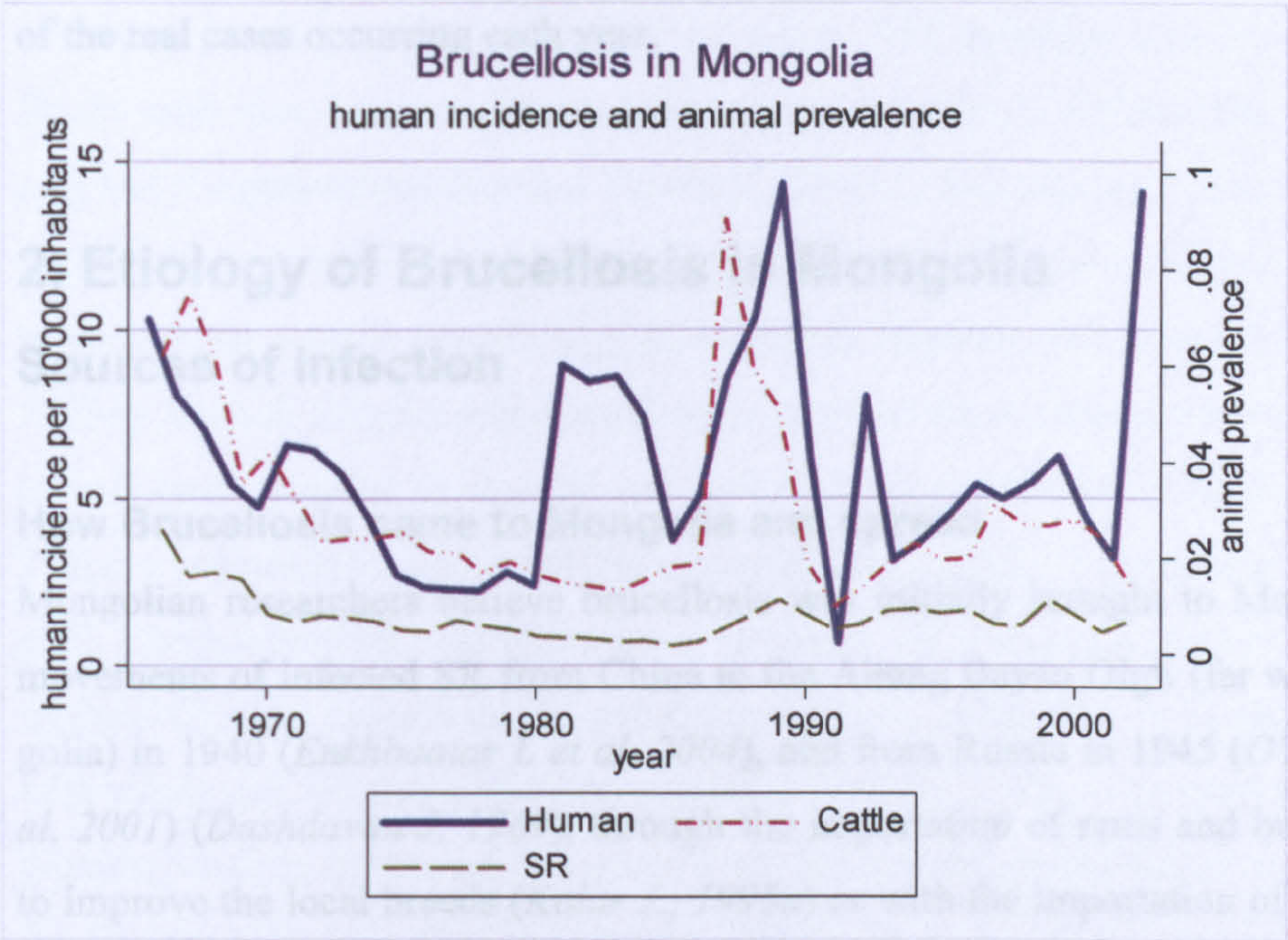
Figure 4.2.: Brucellosis prevalence in animals



Derived from material collected for this thesis

In conclusion, brucellosis in humans and animals has been present over the entire observation period. Owing to its zoonotic nature, animal-human disease trends have mirrored each other: declines in the late 1960s and 1970s, and a volatile and unclear situation in the 1980s, and finally, an increase in the 1990s (figure 4.3.).

Figure 4.3.: Brucellosis in Mongolia: human incidence and animal prevalence



Derived from material collected for this thesis

Brucellosis serological surveys in humans

In the 1980s and 1990s, the authorities conducted several extended surveys among the population and particularly among the population at risk as herders and persons working with livestock. The survey conducted by the State Dispensary of Infectious Diseases, between 1984 and 1989 in 14 Aimags with 46,731 persons, confirmed that brucellosis in humans was a serious public health issue (Enkhbaatar L et al, 2004): 16.5% of the persons tested were under suspicion of infection, 4.5% were confirmed as chronic brucellosis cases, and 3.83% were identified as new brucellosis cases. This high level of infection in humans still remained in the 1990s. Indeed, among

43,758 persons tested between 1990 and 1998, 25% were positive for antibodies and 10% had active brucellosis (*Garin-Bastuji B., 1999*). The further testing of 40,000 herders and persons working with livestock, in the second half of the 1990s, confirmed this picture: 16.1 % showed seropositive reactions and 9.1% had active infections (*State Veterinary & Animal Breeding Department of the Ministry for Food & Agriculture et al, 2001*). This indicates that the officially published incidence rate (*see previous section*), based on reported cases, only represented a small proportion of the real cases occurring each year.

2. Etiology of Brucellosis in Mongolia

Sources of infection

How Brucellosis came to Mongolia and spread

Mongolian researchers believe brucellosis was initially brought to Mongolia from movements of infected SR from China to the Aimag Bayan Olgii (far west of Mongolia) in 1940 (*Enkhbaatar L et al, 2004*), and from Russia in 1945 (*O'Rourke M et al, 2001*) (*Dashdavaa J, 1969*), through the importation of rams and bulls in 1930s to improve the local breeds (*Kolar J., 1995a*) or with the importation of camels. Because imported animals were not controlled, infected animals were brought in (*O'Rourke M et al, 2001*).

The further spread of brucellosis within Mongolia was made possible through cross-breeding between herds from different regions. Traditionally, the herders kept small private herds separate from each other, with little mixing or transfers of animals (*Kolar J., 1995a*). However, with collectivisation: small private herds were fused into larger herds, regardless of health status of the single flocks. In addition, the herders who had become workers of the collective farms still owned a few animals and took these along when changing work to other farms³².

³² Each family was allowed to possess about 50 animals, the privately owned animals were not marked, but the best animals were considered as privately owned (*Roth F., 2003b*).

Relevant animals for the spread of brucellosis in Mongolia

General etiology of brucellosis has been described in chapter 2. The epidemiological studies of the 1960s (see previous section) provided a broad knowledge basis on the relevant animals for the spread specifically in Mongolia. The following were found:

Sheep and goats (SR) were the most important. All strains isolated from SR have proved to be *B. melitensis* (biotype 1 and 3). The infection was chronic in most flocks with many latent carriers and excretors (Kolar J., 1995a). But the abortion rate and the prevalence was low (Kolar J., 1995a). In cattle and yaks, however, the infection was mostly caused by *B. abortus*, although *B. melitensis* strain (biotype 3) has also been isolated occasionally in herds kept together with infected SR (Kolar J., 1970b). Both *B. abortus* and *B. melitensis* were isolated in camels; however infected camels rarely aborted or showed any clinical signs of brucellosis (Kolar J., 1995a). There was little information on the importance of camels in the spread of brucellosis³³. The epidemiological importance of horses, as a source of brucellosis, is very limited. Clinical symptoms are exceptionally rare, regardless of contact frequency with ruminants (Kolar J., 1970b) (Kolar J., 1995a)³⁴. There seemed to be a clear relation between the dissemination of brucellosis in ruminants and in dogs. However the transmission to human is limited in Mongolia as the direct contact between the nomads and their dogs is very occasional (Kolar J., 1970b) (Kolar J., 1995a). Reindeer showed an infection rate of 75% by serological testing in 1984 or 20% in 1985-1986, clinical symptoms could be observed in 13.5% of the animals³⁵. As reindeer are kept only in a limited geographical area (Khuvsgul Aimag) they do not play an important role in the countrywide epidemiology. Mongolian livestock and wild animals live in a close ecological bond. Various antelopes and rodents live and graze on the same pastures as livestock, while wolves, jackals, foxes and vultures accompany

³³ A study carried out in 1966 in 15 Aimags showed an average infection rate of 1.6% among 65,074 camels. The inter-Aimag range of infection was 0.6% to 5.1%. However, 48.9% of the farms had infected camels, with a range varying by Aimag from 11.1% to 81.8% (Tserendash Choijiljav, 1972).

³⁴ Brucellosis in horses was not common in most farms with infection rates in ruminants of between 0.1% and 5%. A study in 1966 including 10,052 horses showed serological reactors in 121 horses (1.2%), which corresponded to a significant lower infection rate than in the other animal species (Tserendash Choijiljav, 1972).

³⁵ All reindeers (717) have been vaccinated with S19 in spring 1986 (Enkhbaatar L et al, 2004).

the nomads to seize weak or sick animals and carcasses or foetuses. Nevertheless a report from 1970 on the principal epidemiological features of brucellosis under conditions of nomadic animal husbandry in Mongolia noticed no important significance of wild animals on the spread of brucellosis in livestock: "Although there are theoretical assumptions and positive findings in many countries, the importance of wild animals in brucellosis epidemiology cannot be considered as high."(*Kolar J., 1970b*).

Thus the epidemiological studies lead to the conclusion that the focus has to be set on SR and cattle (yaks).

Animals relevant for the transmission of Brucellosis to human

Scientific research carried out late 1960s and early 1970s concluded that the incidence of brucellosis in humans may be more closely linked to the prevalence in SR than in cattle and yaks. This conclusion had been drawn on the basis of observation rather than on sophisticated statistical or serological analysis: patients attending the brucellosis dispensary in UB between 1966 and 1971 were workers in farms breeding SR rather than workers in cattle farms (*Tserendash Choijiljav, 1972*) (*Baldanderj T, 1972*). Another observation was that, in Aimags with high SR prevalence rates, human infections seemed higher. This did not appear so clearly for cattle and yaks (*Tserendash Choijiljav, 1972*). Further analysis showed also an association between human incidence and the population size of SR and their density in pasture (*Baldanderj T, 1972*). However there is also scientific research concluding that there was 4–5 times more transmission of brucellosis from cattle to human than from SR to human, but the infection got from SR was more important due to the severity of *B. melitensis* (*Dashdavaa J, 1969*). In early 1980s it had been specified in scientific research the fact that the infection rate of herders dealing with SR ($27.7 \pm 0.96\%$) was higher ($p < 0.01$) than of herders dealing with other types of animals ($11.5 \pm 0.73\%$), even though the prevalence rate of SR was lower than in cattle and yaks

(*Tovuugiin Gombosuren, 1982*). This has been related to the greater number of SR³⁶. In fact it was concluded that 40.5% of the patients were infected by SR, 11.0% from cows, and 29.4% from mixed herds.

Factors influencing Brucellosis transmission

Traditional Mongolian practices have controlled food borne transmission of brucellosis from animal to human: milk was mostly not drunk in its natural state, but transformed to various typical drinks or foodstuffs, which have a preventive effect on the transmission of brucellosis. Usually milk is added to green tea and boiled (called: *Suutei Tsai*), or other milk products are prepared from heated milk (at 70° to 90° C), and leavening is added. Examples are *Urum* (clotted cream), *Tarag* (sour milk), *Byaslag* (soft cheese), *Aaruul* (dried cheese). The only product prepared from fresh milk is *Airag* (fermented mares' milk, also called *Kumys*), but the high acidity arising during the fermentation process (pH 4.2 – 3.9) destroys all *Brucella* organisms within 24 hours (*Kolar J., 1970a*). Naturally, animal husbandry has played an important role in the transmission of brucellosis between animals and from animal to humans. Even though modern husbandry methods have been introduced, such as dairy cattle farming, the bulk of animal production largely remains nomadic or semi-nomadic to this day. Crucial factors in this setting, from an epidemiological point of view, were (i) the close contact between animal and human, (ii) some specific management practices and (iii) the possibilities and habits concerning hygiene. The various opportunities for transmission had been studied in the epizootiological survey in the frame of the "WHO project Mongolia 0001" (see above) and had been listed below (*Kolar J., 1970a*) (*Kolar J. et al, 1968*) (*Cvjetanovic V. et al, 1968*).

Limited data is available on the influence of ecologic changes on brucellosis transmission. This topic seemed to be neglected in literature and will not be treated in

³⁶ It confirms our analysis in chapter 2: we had compared the Mongolian epidemiological situation with this one of the countries in the Near East region. It became evident how in Mongolia the incidence in human was extraordinary high compared to the prevalence in SR.

depth in this thesis³⁷. The pasture land in Mongolia is primarily arid and semi-arid steppe. The climate is harsh and the growing season is short. The pastoral livestock system must be adaptive to these conditions and is very vulnerable to ecological changes. “High levels of climate variability in precipitation occur and it is likely that climate variability in terms of “*Dzud*”³⁸ and drought frequency and intensity will be increased as a result of climate change” (*van Hezik C M E, 2002*). Climate changes deteriorate both yield and biomass of pastures, which finally may lead to animal weight loss and to increasing the vulnerability for disease.

Management practices

(i) The transmission of infectious diseases from one kind of animal to the other was made easy by the fact that various kinds of farm animals were kept together in pastures or at watering places. In this context keeping sheep and goats in common flocks was for the transmission of brucellosis of great importance: the infection in such flocks was sustained, as goats had a higher susceptibility to brucellosis and the carrying and excreting of *Brucella* organism was latent and prolonged.

(ii) Herders do not apply grazing control or fencing. As the pastures are circulating ground for the infectious agents, this favours also the transmission between livestock and wildlife.

(ii) The animals had been moved from various parts of Mongolia to slaughterhouses in UB or to export bases at the border. This favoured the spread of communicable diseases, as the epizootiological situation of the territories passing through had not been considered.

(iii) The animals had been mixed and regrouped frequently. For example the herders brought their private animals to the state herds when moving from one to the other

³⁷ However, Lin and Li (*Lin D X et al, 2000*) reported on the possible links with the El Nino phenomenon in a Chinese paper (*Dequi S et al, 2002*). Based on animal and human brucellosis data from 1949 to 1981, they found higher incidences of SR and human brucellosis during La Nina year. They correlate this to atmospheric changes such as lower temperatures, heavier winds, snow, droughts, and flooding. These, in turn, can be responsible for lack of water or grass, and increased pressure on animals whose resistance against diseases is lowered.

³⁸ Dzud, a Mongolian term, refers to a variety of winter conditions that destroys or prevents access to grazing material, preventing animals from eating and thus surviving during the winter months from October to May. Conditions that lead to Dzud include heavy snowfall (white Dzud), the formation of an impenetrable ice layer over pastures (ice Dzud), or a lack of sufficient winter fodder for animals following summer drought (black Dzud).

working place. Or the dairy cows had been held during summer time on pastures around the centres. However the health situation of the herds has never been considered.

(iv) Usually the aborting animals had not been separated from the flocks.

(v) The rams and bucks had been kept in separate male-flocks and had been distributed for the mating season: this had favoured the spread of brucellosis over large territories.

(vi) Before the mating season the maternal flocks had been completed with yearlings: this had maintained the chronic infection.

Close contact

(i) To protect new born animals from extreme frost it was the practice to bring them into the human habitation (ger).

(ii) The herders skinned stillborn animals to get the pelt or applied the traditional way of slaughtering the SR by avoiding bleeding. Both practices created possibilities for transmission.

(iv) Places as shelters, where animals were kept close together, were littered with dry faeces, contaminated when infectious abortions occurred. These faeces were transformed into fine dry dust, whirled by constant winds and creating a dangerous source of airborne infection.

Hygienic habits

(i) During the winter season the herder had only little water at its disposal, as it had first to be melted from ice. The water was used primarily for drinking and cooking and not for washing and cleaning. This lead to minimal hygienic measures just during the period when abortions occurred and mass-parturition happened. The equipment and shelters could not be cleaned and disinfected. Contact infection had been additionally favoured by hand, often chapped as a result of frost.

Routes of transmission

Human infection through animal contact

Mongolian scientists, such as Smirnov S. M. in 1958 (*Dashdavaa J, 1969*) had recognised early the importance of animal contact transmission over food borne transmission for human infection. Later on, further studies confirmed this: $94.3\% \pm 0.6\%$ of human infections were caused by animal contact and $5.7\% \pm 0.5\%$ by alimentation (*Baldanderj T, 1972*). The importance of contact transmission has again been confirmed by later studies: 89.2% of human infection was due to direct animal contact (62.1% of these during animal birthing season), 4.3% was due to contact with contaminated animal products and only 6.5% of the human infection had been identified as food borne (*Dashdavaa J et al, 1981*). Thus the main risk group has been identified: people having close contact to animals or working with animal products.

Occupational risks for Brucellosis infection

In the 1970s, scientific studies attested that 39% of the herders were infected with brucellosis, 6.6% of the students of Agriculture Institute and 2.2% of the workers of the plants processing wool, leather or meat (*Damdinsuren L, 1972*). Most of the herders were breeding SR or cattle (*Baldanderj T, 1972*). A surveys in urban setting showed very high brucellosis prevalence among workers in plants processing animal products ($50.8\% \pm 6.2\%$ seropositive by allergic test; $20.3\% \pm 3.0\%$ by SAT and CFT) and relatively low prevalence of 1.9% among unprofessional city residents (*Baldanderj T, 1972*).

Surveys conducted in late 1980s reported that 13.5% of the herders were sero positive (*Ministry of Agriculture et al, 1991*), and confirmed the severe contamination of persons working in further high risk professions: 28.7% of the persons working in slaughter houses were infected with brucellosis, 17.8% working in dairy cattle farms, 19.6% working in leather industry and 22.5% working in the wool industry (*Enkhbaatar L et al, 2004*).

This situation seemed to become even worse in the late 1990s, when a survey conducted in 1996 among 42,000 members of the high risk group (herders, veterinarians etc.) showed that 30.9% of them were infected (*Ministry of Food and Agriculture, 1996*).

Epidemiological characteristics

Epidemic season

The course of infection in SR was seasonal with a maximum in May (*Dashdavaa J et al, 1981*). Though most dangerous in epizootic and epidemiological relations was the lambing season, which was in February / March: “The morbidity in human population clearly coincides with the lambing and kidding season, where 80% of all cases of human infections are recorded” (*Kolar J., 1970b*). This goes in line with other analysis showing that 70% of new human infections occurred between March and July (*Baldanderj T, 1972*). However intense human infection has been documented at autumn as well (*Tserendash Choijiljav, 1972*). This confirmed that apart from the lambing season further opportunity of humans to get infection by contact were also with milking or slaughtering of infected animals, both more relevant in late summer and autumn.

Demography

About two thirds of the patients were men (*Damdinsuren L, 1972*). In the urban context however, including the non-professional group into the study, the difference between sexes disappeared (*Baldanderj T, 1972*). In the urban context patients were on average 10 years younger than in rural context (*Baldanderj T, 1972*). This is because students, involved in herding during summer time, belonged to the high risk group, and students were considered urban citizens (*Dashdavaa J, 1969*) (*Tserendash Choijiljav, 1972*). The percentage of infected herder increases with their

age (*Baldanderj T, 1972*). However it has been observed that immunity³⁹ of herders, who have permanent contact with animals, could be sustained for a longer period of time (*Tovuugiin Gombosuren, 1982*).

Predominant strains

The strains isolated from aborted fetuses and milk (*Baldanderj T, 1972*) were biotypes I of *B. abortus* in cattle (*Tovuugiin Gombosuren, 1982*) and all three biotypes (I, II & III) of *B. melitensis* in SR (*Tserendash Choijiljav, 1972*) (*Cvjetanovic V. et al, 1968*). Human studies from 1964 to 1966 and 1975 to 1976 confirmed that most infection in human belonged to *B. melitensis* (*Dashdavaa J et al, 1981*) (*Tovuugiin Gombosuren, 1982*). *B. melitensis* was common in SR, but the migration to cattle occurred sporadic (*Tserendash Choijiljav, 1972*) or with growing role (*Baldanderj T, 1972*).

Chronic versus acute

The analysis of patients diagnosed with brucellosis, between 1958 and 1969, showed that about 70% had chronic brucellosis at the time of diagnosis (*Baldanderj T, 1972*). Later, in the early 1970s, 86.7% of the brucellosis patients had chronic disease (*Damdinsuren L, 1972*). Brucellosis was often diagnosed too late, probably due to limited access to health facilities for diagnosis and treatment. More recently, between 1999 and 2001, 47.8% of the brucellosis patients, treated at the Infectious Disease Centre in UB, suffered from the chronic form of brucellosis, and a survey among 250 physicians resulted 56.4% chronic cases in their consultancies (16% acute, 20% sub-acute) (*Badarch ULAMBAYAR, 2001*). This high proportion in chronic cases reflected poorly on the quality of access to health care and diagnosis (*Erdenchimeg G. et al, 2001*).

³⁹ Immunity in the sense of not showing any symptoms of infection

3. Limitations and discussion

A review of Mongolian scientific work on human and animal brucellosis was published in 2004 (*Enkhbaatar L et al, 2004*) by Mongolian scientists. Comparing their listing of Mongolian scientific work with the literature we have traced, it confirmed, that we had compiled a comprehensive piece of Mongolian literature on this topic. However, the aspects of epidemiology had been reproduced in a narrative or descriptive way, with little analysis. A contribution of this chapter was to make the Mongolian scientific literature accessible to the English speaking scientific world, and to use it as basis for understanding and analysing the control policy, which is the topic of chapter 5. A further contribution of this chapter was to assemble a comprehensive database providing empirical evidence about the spread of brucellosis in humans and animals at the Aimag level. This database provides the basis for the statistical and mathematical analysis in chapter 6. The current chapter however describes the data with maps and graphs. The data has been cleaned (*methods described in chapter 3*) to make it sound and consistent; however, uncertainties remain concerning data collection methods and epizootiological entities.

Limitation and discussion on data quality

Systematic data collection on the spread of brucellosis in Mongolia began in the mid-1960s onwards, during the T&S campaign aided by COMECON and the WHO epidemiological studies. Most of the collected data for this thesis are generated from so-called “grey” literature, such as unpublished or internal reports of various units within the departments of human and veterinary medicine. This method had to be used for lack of available official statistics, and data consistency therefore suffered. The quality of data for the animal disease was much better than for the human disease. Livestock farming was traditionally a very important economic factor in Mongolia, so there was strong concern about animal health. In the late 1960s, for in-

stance, livestock accounted for over 83% of the GDP of the MPR (*Ministry of Health et al, 1970*).

A limiting factor in the consistency of data could be the mixing of data gained from surveillance with reported data. This could be confirmed for the prevalence in cattle in the years 1987 and 1988. Striking were the variations in the 1980s for prevalence in cattle and the incidence in humans (*see figure 4.3.*). The same graphs but on Aimag level are shown in the *appendix 4.2.* and help in the further analysis of these variations. Looking at the policy papers intense testing⁴⁰ of cattle in 7 Aimags⁴¹ in 1987, with isolating or slaughtering the positive reactors and vaccinating the others⁴² could be confirmed (*Ministry of Agriculture, 1987*) (*Ministry of Agriculture, 1988*). The following year additional four Aimags⁴³ have been added to this campaign (*Badarch P., 1988b*). Finally in *figure 4.4.* it became obvious, that the stated prevalence in the Aimags, where surveys have been conducted, is considerably higher than prevalence in the other Aimags. The numbers in *figure 4.4.* show that by including all Aimags the prevalence in 1987 increased to 9%, while with excluding from the calculation those Aimags, where testing had been conducted, the prevalence rate remained at 1.2%. Therefore it can be concluded that the data from the testing are included in the reference material and mixed with the reported data from other Aimags. In 1988 the prevalence rate dropped again, because of the slaughtering of positives the previous year.

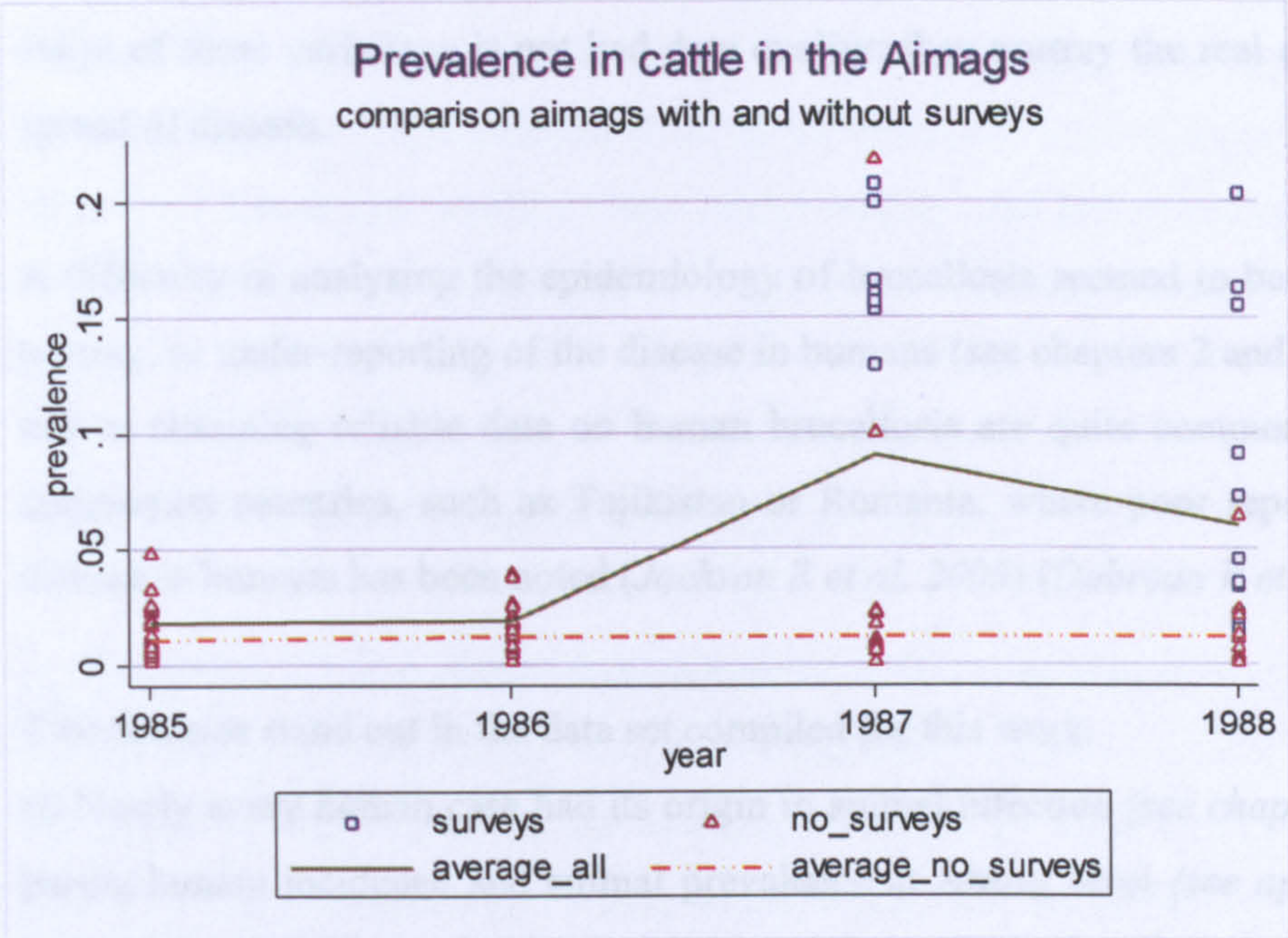
⁴⁰ The diagnostic tests have been performed using SAT, CFT and RB (*Badarch P., 1988b*)

⁴¹ Khuvsgul, Arkhangai, Bulgan, Selenge, Tuv, Dornod, Khentee

⁴² The cattle in two Aimags (Tuv and Selenge) have been vaccinated with S19, the cattle in the other Aimags have been vaccinated using Rev.1 (*Badarch P., 1988b*).

⁴³ Zavkhan, Uvurkhangai, Bayankhongor, Sukhbaatar

Figure 4.4.: The influence of surveys on the prevalence stated



Brucellosis prev. in cattle in Aimags where surveys have been conducted

	1987	1988
Arkhangai	0.200	0.155
Bulgan	0.129	0.018
Dornod	0.208	0.034
Selenge	0.160	0.022
Tuv	0.153	0.035
Khuvsgol	0.165	0.045
Khentee	0.157	0.015
Zavkhan		0.091
Uvurkhangai		0.073
Bayankhongor		0.204
Sukhbaatar		0.163
average:		
<i>incl. Aimags with survey</i>	0.090	0.060
<i>excl. Aimags with survey</i>	0.012	0.012

Derived from material collected for this thesis

A further important issue explaining the variations of the prevalence rate in animals are the so-called “storms of abortions”. This is a typical phenomenon when herds are infected with *Brucella*. With the increasing abortion rate caused by brucellosis, large numbers of *Brucella* are spread into the environment, further increasing the infection risk. Due to high level of susceptibility of the herd, the infection is accelerated until

a certain level is reached, where the proportion of susceptible animals is diminished and the further spread slowed down (*González-Guzmán J et al, 1994*). Thus, the cause of these variations is not bad data quality; they portray the real course in the spread of disease.

A difficulty in analysing the epidemiology of brucellosis seemed to be the poor reporting, or under-reporting of the disease in humans (see chapters 2 and 3). Difficulties in obtaining reliable data on human brucellosis are quite common for former communist countries, such as Tajikistan or Romania, where poor reporting of the disease in humans has been noted (*Jackson R et al, 2003*) (*Dobrean V et al, 2002*).

Two features stand out in the data set compiled for this work:

(i) Nearly every human case had its origin in animal infection (*see chapter 2*). Comparing human incidence and animal prevalence at Aimag level (*see appendix 4.2*) showed that the disease in humans did not follow the course of disease in animals. This phenomenon has also been observed and described in Tajikistan (*Jackson R et al, 2003*) and in China (*Dequi S et al, 2002*). In China it has been called as “separated phenomenon of human and animal brucellosis”. The reason given for the “separated phenomenon” was, that the time, place, tests and sampling methods of surveys on human and animal brucellosis were not standardized and uniform (Shang, 1996) (*Dequi S et al, 2002*). This may explain why this close link of the disease spread in humans to the disease reservoir in animals seemed to be missing. Further statistical analysis on this will be done in chapter 6.2.

(ii) Other phenomenon could also be observed (*see appendix 4.2*): in 1987 and 1988 enormous increases occurred in some Aimags in both cattle prevalence and human incidence. As we will see in chapter 5, it mostly concerned Aimags which had been involved in T&S and vaccination campaigns in cattle. In all but two Aimags⁴⁴ the reported incidence in humans reflected the onset of control activities in cattle⁴⁵. This was shown for the Aimags Dornod, Tuv, Zavkhan, Ovorhangay and with a time lag

⁴⁴ Arkhangai, Bayankhongor

⁴⁵ In Selenge the inc. in human was a year previous to the control activities, so in the preparation phase.

of one year for Bulgan, Khuvsgul, Hentiy and Sukhbaatar (time lag of two years). Policy activities in animals could have lead to more rigour in reporting human data. On top of it, this augmented awareness led, in some cases, to surveys being conducted in humans ⁴⁶ (*Enkhbaatar L et al, 2004*). The results of these surveys may have been mixed with reported cases, which lead to a sudden enormous increase on human incidence, which did in fact not correspond to the real course of disease.

Discussion on the epidemiological entity

In the chapter 2 it was shown that each infected flock poses a risk for public health and therefore the entire flock should be regarded as infected, even if few animals proved to be seropositive. If, for example, there are 10 cases in an Aimag drawn from 10 different herds then because of the contagious characteristics of brucellosis it is likely that all animals are infected or exposed. If the sample was of 10 cases from one herd it provides no information about the prevalence of the disease in the other herds (Question of herd infection). Therefore in brucellosis control, the entity of interest should be the infected herd rather than the infected individual animal. However, the data collected and analysed were related to the reported prevalence in the individual animals.

Some Mongolian scientific literature published figures on the prevalence in herds, and these showed how serious the brucellosis contamination was (*see first section of this chapter*). The prevalence in SR seems to be low (<2%, *see figure 4.2.*), but the surveys conducted in the late 1960s showed that 80% of the SR flocks were infected with *Brucella* (*Kolar J., 1970b*). As shown in the *appendix 4.3.*, the situation was similar in cattle: surveys conducted in 1966 in 307 farms showed that infected cows had been identified in 284 (92.5%) farms. Also on Aimag level, the percentage of farms with infected cattle was very high, and varied from 71.4% to 100%

⁴⁶ According to the results of an epidemiological study and reports from the State Dispensary of Infectious Diseases, the prevalence of human brucellosis was 20.7% in Arkhangai, 31.8% in Selenge, 23.4% in Bulgan and 20.3% in Dornod Aimags between 1987- 1988(*Enkhbaatar L et al, 2004*).

(*Tserendash Choijljav, 1972*). The contamination of herds was evenly spread throughout the country. Another survey conducted in 1983, among cattle farms, showed an individual prevalence between 0.1 and 6.4%, but 52% of all tested farms had infected cows (*Khohoo A. et al, 1995*). “Brucellosis researchers have long been aware that the real epizootiological entity is not an animal population scattered over an entire area, but an *animal herd*, whereas man as the real contact with the animal reservoir must always be evaluated as an individual single case. However, in areas where the common grazing of herds is practiced, the area or village are more like an epizootiological entity than the separate herds” (*Thimm Bernhard M., 1982*). In nomadic conditions, it is difficult to arrange strict isolation of infected herds, and thus the high number of infected herds is a constant danger to the healthy ones. Therefore, animals roaming an area as extended as an Aimag could very well be considered as a single herd entity from the point of view of control policy.

The policy of Brucellosis control in Mongolia

The previous chapter discussed the epidemiology of brucellosis in Mongolia. The spread of brucellosis over space and time in cattle, SR and humans was chartered. The etiological factors determining the sources, factors and routes of transmission in Mongolian context were analysed. This created a comprehensive picture of the brucellosis in Mongolia and allowed an assessment of appropriate control strategies to be made.

This chapter tackles the second aim of this thesis: *“to provide an historical overview on the different strategies applied to the control of brucellosis in Mongolia.”*

Data on the effective vaccination level of cattle and SR had to be traced down from yearly activity books found in the archives of various authorities within the MoA and out of the yearly production books found at the Biokombinat⁴⁷. So the following analysis of the policy of brucellosis control in Mongolia was based on a unique and nearly complete set of Governmental policy papers and on a unique and complete set of data on testing and vaccination.

This chapter begins with a discussion of the relative importance of brucellosis control. This is followed by an historical overview of the policy of brucellosis control, based on policy papers of the Mongolian Government, completed by consulting “grey literature”, published literature, and personal communication.

The changes in the political and economic organisation, during the transition period, when the economy changed from a planned one to a more market oriented one, were amount to the analysis. The effects of these upon the spread of disease and the sur-

⁴⁷ Biokombinat is the Mongolian factory near UB producing the vaccines for animals.

veillance policy have been included. In the third section the historical policy overview is underpinned with data on testing and vaccination.

1. Brucellosis and other animal diseases

Mongolia controlled, eradicated or kept out many animal diseases, that occurred in neighbouring countries (*see chapter 4*). Three elements helped to achieve this (*Honhold N., 1994a*): (i) the extensive grazing systems and low animal density had a favourable effect on the surveillance of rapidly spreading infectious diseases; (ii) the field veterinary services, large and well organised, focusing preventive treatments, had enabled full treatment of all herds; (iii) the Biokombinat factory, producing a wide range of good quality vaccines meeting the needs of the country.

An FAO mission, visiting Mongolia in 1976, stated that there were no official periodic animal disease reports, despite the importance of animal health for the well-being of the country (*Food and Agriculture Organisation of the United Nations, Rome, 1977*). However, the animal health situation encountered had been assessed by this FAO mission as generally good. Foot-and-mouth disease, anthrax and rabies had only low sporadic incidence. The last outbreak of foot-and-mouth disease had been brought under control in 1964. Rinderpest, contagious bovine pleuropneumonia, contagious caprine pleuropneumonia and sheep/goat pox had been brought under control thanks to efficient measures applied during many years. Bovine tuberculosis is said to be not present in Mongolia (*Honhold N., 1994a*). Parasitic and tick-borne diseases were not well documented, but still occurring. Important disease problems however were seen in glanders in horses and brucellosis in various species (*Food and Agriculture Organisation of the United Nations, Rome, 1977*).

For decades, brucellosis has been challenging authorities responsible for disease surveillance. Chapter 4 illustrated how this disease is still not under control. In the 1950s, the disease was studied at random in animals and humans. But still there were no coordinated surveys and no effective prevention and control measures taken.

Since the 1960s, brucellosis has been studied systematically, to enact effective control measures.

2. Review of the Brucellosis control policy history

First attempts at Brucellosis control during 1950s and early 1960s

Nearly every year since 1953, the Minister's Cabinet has issued resolutions to fight brucellosis (*Enkhbaatar L et al, 2004*). In the early 1950s, the focus was on treatment of patients infected with brucellosis, and on prevention for people at risk. The main interest for research was the transmission from animal to human. Brucellosis cases in humans had to be notified to the authorities from 1956 onwards (*Dashdavaa J, 1969*). The following methods were applied to protect herders, veterinarians and workers during the lambing seasons from infection: (i) introduction of hygienic measures such as supplying protective clothing and disinfectants; (ii) vaccination of people with dry and live vaccine (19-BA) before the lambing season (according to common procedures already applied in the Soviet Union).

Later on, from 1957 onwards, the MoA began fighting the disease in animals by applying appropriate management practices and improving hygiene. Measures carried out included screening tests in milk and milk products, testing of all imported animals (mostly for breeding) and supplying of the required manpower and equipment for laboratory facilities (*Enkhbaatar L et al, 2004*).

The first comprehensive measures to fight brucellosis both in humans and animals, followed in 1959 (*Molomjamts et al, 1959*). Both ministries, MoH and MoA, had been ordered to launch a broad public advocacy campaign about the harm of brucellosis and about methods of prevention. This was accompanied by vaccination of SR with the S-19 vaccine.

In 1960, the government decided to plan epidemiological surveys of brucellosis in animals and humans to fight brucellosis (*Dashdavaa J, 1969*). These were put into action between 1963 and 1968 with the assistance of WHO and COMECON (*see chapter 4*).

First attempts to adapt governance structure for Brucellosis control

Meanwhile in 1961, the MoA had established a brucellosis laboratory within the Veterinary Research Institute (VRI) (*Enkhbaatar L et al, 2004*). Nevertheless, the application of veterinary measures in the control of zoonoses was hampered by the fragmentation of agriculture and animal husbandry into four different areas of expertise: animal husbandry, veterinary, agronomy and agricultural mechanisation. This resulted in overlapping and overstaffing of the state administration of collective farms and led to governmental agencies being unclear of their responsibilities (*Cvijetanovic V. et al, 1968*).

Additionally, the MoH had taken some organisational measures and had established in 1962 a Division for Brucellosis within the Infectious Disease Research Institute (IDRI); the purpose was to establish a unified system responsible for fighting and preventing human brucellosis (*Enkhbaatar L et al, 2004*). Before this the various responsibilities for fighting brucellosis, such as investigating, diagnosing and providing therapy, were spread over different institutions. The following year the Division for Brucellosis expanded and became the National Epidemiological Unit which acted as the cooperating counterpart of the WHO epidemiological group (*see chapter 4*). In 1966, the government established the National Dispensary against Brucellosis within the MoH (*Ministers cabinet of Mongolia, 1966a*), which was responsible for the methodology and organisation of prevention and treatment of brucellosis (*Khohoo A. et al, 1995*) (*G.Kupul, 1972*).

Though it was well-known that the major public health problems were zoonoses and food borne infectious diseases, there was still little organised cooperation between the veterinary and public health services in the areas of health legislation, environmental sanitation, control of zoonoses, food hygiene, production of biologicals, scientific work, and training of public and veterinary health personnel (*Cvjetanovic V. et al, 1968*). And so the Mongolian Government had continuously taken decisions for developing adequate governance structures to ensure the quality and methodology of prevention, diagnosis and treatment of brucellosis and improving the management of brucellosis control. Still it seemed that these efforts went on and on, and no optimal solution for intersectoral governance could be found and implemented.

“Test and Slaughter” policy from 1966 to 1968 with COMECON assistance

The first widespread large-scale control measures began in 1966 (*Khohoo A. et al, 1995*) with assistance given by COMECON States whose purpose was to combat the three main zoonoses: brucellosis, tuberculosis and glanders. At that point, the Mongolian authorities had fully realised, that prevention of human brucellosis lay mainly in the control and eradication of the disease in animals (*Jezek Z. et al, 1969*) (*Tsedenbal, 1965*). The programme started in 1966, and continued for three years during the summer and autumn.

The goals given to the COMECON veterinary groups, working in close cooperation with the local veterinary services, were (*Jezek Z. et al, 1969*) (*Kolar J., 1970a*):

- (i) to examine all the susceptible adult animal population for brucellosis, tuberculosis and glanders;
- (ii) to isolate the reactors if possible or to slaughter them;
- (iii) to work out plans for control measures for each Soum and Aimag.

The mobile laboratories of the COMECON groups were well-equipped for carrying out serological investigations, especially SAT and CFT.

The eradication campaign was based on the opinion, that repeated testing and slaughtering or isolation of reactors would lead to reduction and finally to eradication of brucellosis in livestock. To conduct this enormous work, between 1966-1968, 10 to 12 millions animals were tested yearly⁴⁸ (*Kolar J., 1977*). As a result, the number of individual sero-positive reactors was reduced by 54.4% in sheep and 31.2% in goats (*Baldanderj T, 1972*). But the decrease in the number of infected flocks was much slower as re-infections occurred often (*Kolar J., 1977*). Until 1973, data from this campaign was evaluated to implement hygienic measures and to train persons at risk (*Ministers cabinet of Mongolia, 1969*). Sadly, it became obvious, given local conditions and the limited reliability of the diagnostic tests used, that no permanent success could be expected (*Kolar J., 1970a*).

The T&S method, applied by the COMECON States proved to be ineffective and failed to control brucellosis. The available diagnostic tests (allergic skin test, SAT, CFT) had limited reliability, as they had difficulties to reveal infected animals in the latent phase of disease (*Kolar J., 1995c*). The allergic skin test had been used, as it was easy to perform in nomadic and semi-nomadic conditions, and did not require identification of tested animals; furthermore, the result can be read after two days, and the reactors could immediately be marked. In doubtful cases, the examination could be repeated in SAT or CFT (*see also chapter 2.4. on testing methods*). The T&S method applied to individual reactors may have resulted in considerable reduction of them within the tested flocks, but not in the definite elimination of the disease from the flock itself. For the T&S method to be effective, the slaughter should have been applied to the entire flock. Such a radical procedure would have been suitable to get rid of brucellosis when implemented into a previously non-infected region (for instance by imported animals) (*World Health Organization et al, 1986*). It would have meant an immediate eradication at any cost. However, in the Mongolian context, with large flocks and high prevalence of brucellosis, this was not practical due to high costs and the difficulty of replacing stock with healthy animals (*Kolar J.,*

⁴⁸ Between 1966 and 1968 totally 37.5 million animals had been tested (*Ministers cabinet of Mongolia, 1969*).

1995c). The Mongolian Government decided therefore, after the failure of the T&S method, to abandon it and to switch to whole herd vaccinations (*Kolar J., 1995c*).

WHO project “Mongolia 0001”: surveys

Epizootiological surveys, assisted by WHO experts, have been carried out since 1963 (*see chapter 4.1.*). An objective comprehensive analysis of the complicated epizootiological situation in animal brucellosis had considered the practices and habits of local animal husbandry, the possibilities with the available manpower, and the economical constraints. This led to the conviction that in the prevailing conditions only systematic large-scale vaccination simultaneously with other basic control measures would be effective (*Kolar J., 1970a*).

Since there was practically no experience in the vaccination of SR against brucellosis in Mongolia, this conviction was confirmed after three vaccination field trials, undertaken during the period 1966–68 in the frame of the WHO project “Mongolia 0001”. The aim of the trials was to study the immunological value of *B. melitensis* Rev.1 vaccine in Mongolia against sheep and goats vaccinated with *B. abortus* S19 vaccine, as well as against an equal group of non-vaccinated animals (*Jezek Z., 1970*). Thus, both vaccines used in the trial showed significant protection, but more significant results were obtained with the Rev.1 strain compared with S19, and the conclusion was that the protective efficacy of Rev.1 vaccine in local breeds of SR was considered as satisfactory.

The immunisation of cattle (calves, heifers and cows) with S19 vaccine against *B. abortus* was only satisfactory in some herds. Isolations of *B. melitensis* in other herds, where abortions continued to occur after vaccination with S19, led to the consideration of the Rev.1 vaccination instead of S19. A controlled comparative trial on 200 heifers was carried out in October 1968 in order to dispel the fears that Rev.1 may cause infection in cattle and in subsequent excretion in milk. It was proved that the Rev.1 vaccine was effective against both strains, while S19 provided signifi-

cantly less protection against *B. melitensis* (Kolar J., 1995c). This result led to the subsequent application of Rev.1 vaccine for the immunisation of cattle and yak population, without any negative effect. In addition, in connection with the planned brucellosis vaccine production in Mongolia, it was desirable, to avoid laboratory complications and to simplify production procedures, to produce only one vaccine, namely Rev.1 (Kolar J., 1970a). The Mongolian application of Rev.1 for the immunisation of cattle was unique in an international context (*see also chapter 2.4.*): “Wide use of Rev.1 vaccination in cattle, with the unique intent of obtaining protection against *B. melitensis* infection, has been applied only in Mongolia” (Banai M, 2002).

Summing up, the trials had produced clear evidence that vaccination, especially with Rev.1, was highly effective in local Mongolian breeds and in nomadic farming contexts. This method of control was also more reliable, simpler and cheaper than the repeated examination of flocks, and isolation of animals (Cvjetanovic V. et al, 1968). Considering these facts, the MoA decided to approve mass vaccination of cattle and SR. This decision represented an important milestone and a qualitative change in the achievement of control of brucellosis in Mongolia (Cvjetanovic V. et al, 1968).

WHO Project “Mongolia 0013”: vaccine production and vaccination campaign

Assuring Rev.1 vaccines

The Rev.1 vaccine used in the above vaccination trials had been provided by professor Sanford S. Elberg (Roth F., 2003b), one of the developers of this vaccine (Elberg S. et al, 1956). The *B. abortus* S19 vaccines could be acquired from the USSR (Tserendash Choijiljav, 1972). But no laboratory in the world could assure the production of the required amount of Rev.1 vaccines at a reasonable price. Finally, in 1973, the UNDP agreed to assure financial support for building up a local brucellosis vaccine production unit, when WHO took over the responsibility of its technical realisation (Kolar J., 1995b). The whole herd vaccination programme had a long-

term projected existence of 11 years, until 1985. WHO & UNDP assured financing and technical assistance for 5 years until 1977, to build up local vaccine production and to start the vaccination campaign. After overcoming some difficulties, the Mongolian production of Rev.1 vaccines finally began in 1975 in the buildings of the Biokombinat (*Kolar J., 1995b*).

The dried Rev.1 cultures for preparing local stocks of cultures for seed material had been provided by two reference laboratories (*World Health Organization et al, 1964*): (i) from the Central Veterinary Laboratory in Weybridge, England in 1974 and (ii) from the Department of Bacteriology at the University of California (Prof. Elberg) in Berkeley, USA in 1976 (*Kolar J., 1977*). Quality assurance was performed within the country by the independent State Control Laboratory for veterinary biologicals, and also performed abroad in Moscow ⁴⁹ and Weybridge (*Kolar J., 1995b*). The number of living *Brucella* organisms per dose was kept between $1-3 \times 10^9$, which corresponded to the FAO/WHO recommendations (*World Health Organization et al, 1964*). It was planned to increase the vaccination production according to the requirements of the vaccination scheme, with a production peak of 5.5 million doses in 1980 (*Kolar J., 1977*) (*Kolar J., 1984*). The vaccines were stored below zero, and transported to the Aimag Centres by Airplane. The distillate water needed for dilution was brought by lorries. The plan was to vaccinate about 31 million animals with Rev.1 during the period of eleven years (1975 to 1985) (*Kolar J., 1995c*). The territory covered by the immunisation process expanded gradually determined mostly by the vaccine's availability. The maps in *appendix 5.1* show the yearly vaccine programme's expansion.

Strategy for eradication of Brucellosis

The vaccination programme concerned the immunisation of mainly SR and few cattle (*Ministry of Agriculture, 1975*) (*Ministry of Agriculture, 1976*). The trials carried out in 1968/69 with the immunisation of cattle with Rev.1 were taken to a larger scale in 1977 with the vaccination of 80,000 cattle with Rev.1 and produced good

⁴⁹ WHO Brucellosis Reference Laboratory, Institute of Microbiology and Epidemiology, Moscow

results (*Kolar J., 1977*) (*Dashdavaa J et al, 1981*). The vaccination of cattle (with S19 and Rev.1) was only at low and decreasing levels. However, the whole herd vaccination campaign concerned the immunisation of SR and started in year 1975 in two Aimags (Bulgan & Selenge). The maps in the *appendix 5.1.* show how every year additional Aimags were added to the programme, until 1980, when all female SR were immunised nationwide.

The vaccination scheme included in the first year all female SR, and in the following 5 to 6 years, replacements and new born animals, until the flocks were completely renewed. At this stage, the immunised flocks would be tested and the reactors eliminated; the control method would then switch to T&S (*Kolar J., 1977*).

Introducing new procedures in vaccination

There was general agreement that Rev.1 was the best available vaccine against *B. melitensis* infection. However, the methods for using this vaccine in whole-herd vaccination campaign were a continuous source of controversy (*Mustafa et al, 1993*). The specific Mongolian natural and ecological conditions, the local animal husbandry practices, and the considerable countrywide level of brucellosis prompted the project team and Mongolian authorities to apply previously un-validated procedures in the following ways (*Kolar J., 1995c*):

(i) All female animals, regardless of age, pregnancy, and brucellosis status, had been considered for vaccination. The conventional way of immunisation with live *Brucella* vaccines however were limited to young animals. This was to minimise the diagnostic problems of stimulated post-vaccine antibodies confusing the interpretation of diagnostic tests, and also to prevent possible abortions induced by the vaccines. However, this was not important in Mongolia because nearly all the flocks were already infected and the control was no longer based on T&S policy (*Kolar J., 1995c*). To avoid vaccination during pregnancy, which could provoke abortion in infected animals, the vaccination period had to be chosen carefully: under extensive management conditions, SR have known lambing seasons, offering an ideal time

window for vaccinations (*Blasco J M, 1997*). Breeding takes place in September/October, and lambing in February/March. Therefore, the vaccination of young and adult animals can take place four months after birth and before breeding, in July/August. To limit vaccination to sexually immature female animals was impracticable in Mongolia, and could not minimise the source of infection, allowing it to spread freely among non-immunised adult animals, prolonging the recovery period in flocks, and complicate the control process (*Kolar J., 1995c*).

(ii) In common practice pre-vaccination testing would have been applied. But this was unfeasible with nomadic husbandry, and did not increase efficacy and safety. It was therefore abolished in 1977 (*Kolar J., 1977*).

(iii) It was generally proposed as the only reasonable method in terms of safety and efficacy to use conjunctival route of vaccination in whole herd vaccination of SR (*Blasco J M, 1997*). This vaccine administration method has the advantage over the subcutaneous administration that it does not induce a lasting serological reaction and allows therefore the serological monitoring of vaccinated flocks (*Food and Agriculture Organisation of the United Nations Rome, Italy, 1992*). Under Mongolian environmental conditions however using the conjunctival route would have resulted in unacceptable potential exposure of the people involved in the vaccination because of permanent strong winds and inappropriate safety equipment (*Mikolon A.B., 2000*). Therefore the subcutaneous route of administration had been applied and not the conjunctival.

(iv) Traditionally it was unusual to vaccinate breeding males with Rev.1. However after studying in field trials, the effect of the Rev.1 vaccine to spermatogenesis, fertility and orchitis risk (*Kolar J., 1977*), the vaccination of breeding males two months before breeding season had been applied countrywide (*Kolar J., 1995a*). Breeding males were kept strictly separated in male flocks, but became infected with brucellosis when put into infected flocks for breeding (*Kolar J., 1995c*). Because of the importance in the epizootiology of brucellosis the immunisation of breeding males was strongly demanded (*Kolar J., 1995a*).

(v) A dose of one billion bacteria (1×10^9) for young SR (*Mustafa et al, 1993*) was recommended for subcutaneous administration at that time (between one and two billion bacteria per dose before (*World Health Organization et al, 1964*)). In an effort to use less vaccine, trials with reduced doses of Rev.1 were carried out in 1975 in 5000 animals among 8 flocks. This would enable the speeding up of the immunisation process, reduce the cost of production, and lessen the risks of abortions, shorten excretion time, and persistence of post-vaccination antibodies (*Kolar J., 1977*). Results showed no difference between a doses of two billion bacteria (2×10^9) and doses reduced 10 times or even 100 times. However, the Mongolian expert's panel refused to apply such a reduced dose. This proved prescient, as control testing of batches stored at temperature of 10–15°C for 1-3 months showed a decrease in viable cells of 1/3 to 1/12 of the original level (*Kolar J., 1995b*). Vaccines with reduced dose would have lost their efficacy.

From 1975 to 1997/98 Biokombinat produced Rev.1 vaccines with 2 billions bacteria/dose (2×10^9). After 1998 they reduced it to (1×10^9). Noteworthy since the middle of 1980s WHO has recommended this reduced dose (1×10^9) and has always asked the Mongolian Government to follow this recommendation. But the Mongolian authorities did not follow this recommendation until 1997/98 for the following reasons: (i) the vaccination period is in the warm season, and the Mongolians had problem with the cold chain; (ii) also the veterinarians were not feeling responsible enough to care about the correct storage and application of the vaccine; (iii) there was also the practical problem of not working precise enough and so the potential risk for the veterinarians applying instead of 1 ml vaccine liquid only 0.8 ml by mistake. Finally in 1998 the WHO recommendation had been followed for two reasons: (i) because of the decreasing economical situation (reduced dose is cheaper) and (ii) because of political reasons, the WHO was steadily insisting to follow its recommendation and Mongolia had joined WTO in 1997 (personal communication with Sodnom BYAMBA, former leader of Brucellosis vaccine production at Biokombinat (*Roth F., 2003a*)).

Summing up, the Mongolian whole herd vaccination campaign provided new information concerning the effective application of Rev.1, which became an important basis for future vaccination campaigns worldwide (*Kolar J., 1995c*). Since, the vaccination of all susceptible animals, irrespective of age, gravidity and serological status, has been widely proven and generally accepted. Vaccination was expanded in the 1990s to sexually mature females, using reduced doses ^{50 51} (*Banai M, 2002*). The immunisation of breeding males in heavily infected areas has been considered if they are used for natural service. Otherwise, it is not recommended as vaccine strains can be localised in the genital tract (*Banai M, 2002*). Additionally, other Mongolian practices, such as the use of Rev.1 in cattle, have not been approved for common practical use (*Banai M, 2002*).

Governance

The Mongolian Government established an inter-ministerial committee between the MoH and MoA for coordination and periodic control of the programme's accomplishments. The animal health control was centrally organised and supervised by the Veterinary Department (MoA). A new Brucellosis Unit had been established within this department for the management, implementation and supervision of the field vaccination work (*Kolar J., 1995b*). The large-scale vaccination was executed by veterinary brigades, composed of veterinary assistants and assisted by Soum veterinarians. This organisation seemed to be efficient for the vaccination campaign (*Food and Agriculture Organisation of the United Nations, Rome, 1977*). The unit to fight human brucellosis become an independent medical preventative organization, a State Dispensary of Brucellosis, with mobile group branches (*Ministers cabinet of Mongolia, 1977*) (*Ministry of Health, 1977*). Thus, the responsibility for the execution of

⁵⁰ The lowered doses resulted in lower antibody titres which receded rapidly, and therefore do not disturb testing. Diagnostic tests, such as ELISA, are able to differentiate antibody classes (*Erdenebaatar J et al, 2004*).

⁵¹ Recommended cells per dose:

Rev.1 in SR at age 4-6 months by subcutaneous administration or conjunctival instillation: (1×10^9);

Rev.1 in adult SR by subcutaneous administration: reduced at ($5-10 \times 10^4$);

S19 in calves at age 4-12 months by subcutaneous administration (3×10^8 to 3×10^9);

S19 in adult cattle by subcutaneously administration (3×10^8 to 10×10^8);

S19 in adult cattle by conjunctival instillation: ($5-10 \times 10^9$).

(*World Health Organization et al, 1986*)

the project's activities had been distributed between the MoH and the MoA. However, the overall responsible executing agency was the MoH as counterpart of the WHO, and the MoA was left as collaborating agency. This mixed system led to some conflicts in determining the duties and competence of both ministries (*Kolar J., 1977*).

Conflicting too was the collaboration among the international funding organisations. The withdrawal of UNDP's assistance, in mid 1976, had a great impact, but the project was rescued by WHO until the end of 1977. The FAO then took over financing technical assistance in 1978 (*Kolar J., 1978*). The vaccination campaign started later than planned, so there was only 2 ½ years left for WHO's assistance (1975 to 1977).

Evaluation

WHO experts affirmed in 1978 that the immunisation campaign had had a positive impact. They noticed a drop in abortion rates in the vaccinated Aimags, compared to those Aimags not yet included in the vaccination campaign. The best evidence of the vaccination's benefit seemed to be the drop in human brucellosis incidence in all vaccinated Aimags (*Kolar J., 1977*). Strict post-vaccination controls were carried out in about 15% of the flocks (randomly selected) to fight against faulty vaccination or cheating, but also to evaluate the vaccine's quality. This revealed rather different percentages of reactors, depending on which team carried out the vaccinations. On average, the vaccination coverage was lower than 95%, owing to improper vaccination (*Kolar J., 1977*). It was admitted however, that for more advanced analysis on the evidence, effectiveness and benefit of the vaccination campaign longer observation period, further sampling, and more information based on facts would be needed (*Kolar J., 1995c*).

In 1977, an assessment financed by FAO reported problems possibly compromising the programme (*Kolar J., 1978*): (i) The vaccination programme had remained without central project leadership and responsibility, as the counterpart and local project leader, Dr. Basan, had been transferred to the countryside; (ii) the newly created

Brucellosis Unit at the Central Veterinary Laboratory was entrusted only with the control of a few dairy farms around UB, limiting its nationwide access; (iii) no evidence on the effectiveness was available because no post-vaccination controls had been performed; (iv) The 1978 vaccination campaign had not been appropriately prepared.

Since 1978, no further official information on the achievement of this immunisation campaign is available. However looking at the maps in *appendix 5.1.* or at the *figure 4.2. (chapter 4)* one notices the success of this campaign, and while it lasted, the prevalence of brucellosis in SR was generally lowered nationally.

Surveillance 1978 to 1990

Continuation of the vaccination campaign in SR

This research found no further Government resolutions or reports concerning the animal vaccination campaigns launched by WHO and UNDP in 1975. The campaign was supposed to continue from 1978 onwards without international assistance, up 1985. However, key persons interviewed did confirm that this vaccination campaign had been followed up. Our data search in the archives of the MoA brought us the only written evidence proving that the vaccination campaign had actually been followed up: in the yearly activity books, which contained unpublished material, we could trace the yearly planned, as well as the effectively executed, vaccination for cattle, sheep and goats for every Aimag. It gave evidence that the campaign had been continued with the vaccination of about one fifth of the SR-population, which might correspond to the new born animals as the key informants confirmed (personal communication with Dr. P. CHULUUNBAATAR (*Roth F., 2003a*)). A different key informant stated that all young animals had been vaccinated once a year and additionally all adult female animals for many years (personal communication with Prof. Dr. A. YONDONDORJ (*Roth F., 2003a*)). But this did not correlate with the data on the effective vaccination found in the activity books.

Protecting humans

The MoH strived in 1977 to establish a mutual exchange of experiences in fighting brucellosis with the Kazakh State (*Ministry of Health, 1977*), then part of the Soviet Union. Two years later, this exchange was to be expanded to a scientific collaboration with the Research Institute of Microbiology and Infectious Diseases (*Ministry of Health, 1979*). This collaboration has been initiated from the human medical sector. It was aimed to protect workers exposed to infection risks with measures such as vaccination and improving hygiene by providing protecting equipment.

Excursus: Preventative vaccine against Brucellosis in human

Today, vaccination of humans plays only a small role worldwide in the prevention of human brucellosis infections (*see footnote in chapter 2.4.*). In the past, however, various vaccines have been used in humans, mainly in the former Soviet Union and China, but also in France (*Corbel M J, 1997*). Since 1952, workers in the USSR exposed to *B. melitensis* have been immunised using the live vaccine *B. abortus* 19-BA, derived from *B. abortus* strain 19 (*World Health Organization et al, 1986*). The Chinese used *B. abortus* strain 104M, a more virulent strain. In France, to protect exposed people, non-living vaccines had been administered, but the efficiency and the duration of the resulting immunity were not satisfactory. In cases of live vaccines, serious potential risks, such as reactions in individuals sensitised by previous exposure to *Brucella*, led to limited applications. The Mongolian authorities applied the live attenuated *B. abortus* strains 19-BA, which has been provided from Russia, and also used there. The good results of the first survey, carried out in 1957 with 200 workers in animal livestock, were of great epidemiological importance: the immunisation had shown to be successful, and was then applied broadly (*Enkhbaatar L et al, 2004*). The prevention of human brucellosis by immunisation of humans at risk was seen as very important as about 70% of the Mongolian population were working in the livestock sector (*Enkhbaatar L et al, 2004*). The brucellosis prevalence rate of people working in high risk areas with infected animals was estimated between 30-40%, and it was reported that 95% of the vaccinated people had not been infected

(*Enkhbaatar L et al, 2004*). The success of human vaccination in Mongolia was further reported in the 1960s (*Baldanderj T, 1972*) and the 1970s (*Dashdavaa J et al, 1981*) (*Tovuugiin Gombosuren, 1982*). Today there is no human vaccination reported in Mongolia, and it remained unclear, when this vaccination was actually given up.

Russian assistance to fight Brucellosis in cattle

The policy of fighting brucellosis during the 1980s had mainly been focused on preventing food borne infection of the urban population: From 1970 until 1990, dairy farms were established, each containing between 200 and 1200 dairy cows. Since the animals were cramped closely together, special care was necessary to avoid brucellosis transmission (*Khohoo A. et al, 1995*). In 1979, the government ordered the separation of cows infected with brucellosis (Resolution of Minister's Cabinet Nr 29, 26.1.1979, cited in (*Enkhbaatar L et al, 2004*)), as well as hygienic measures for handling the milk (Resolution of the Minister's Cabinet Nr 307, 1979, cited in (*Enkhbaatar L et al, 2004*)). In 1982, the MoA established a special committee responsible in monitoring brucellosis tests to certify farms free of brucellosis (*Ministry of Agriculture, 1982*). In 1986, Mongolia and the Soviet Union concluded an agreement about technical, economic and scientific collaboration from 1986 to 1990 to fight brucellosis in dairy farms in Mongolia (*Ministry of Agriculture, 1986*) (*Ministry of Agriculture, 1987*). Joint Mongolian and Russian expedition teams tested 1.312 million cattle between 1987 and 1989 all over the country to identify the level of infection on Aimag and Soum level and to get proper basis for defining the methods to fight brucellosis (*Enkhbaatar L et al, 2004*). The suspicion that the results of these surveys in dairy farms were mixed with the reported prevalence data on brucellosis in cattle has already been expressed in *chapter 4.3.*. This would explain the peak of brucellosis prevalence in the years 1987 to 1989 as shown in *figure 4.4. (chapter 4.3.)*. As a result 1.218 million healthy cows had been vaccinated with Rev.1 or S19 (*Ministry of Agriculture et al, 1991*) (*Ministry of Agriculture, 1988*) (*Badarch P., 1988b*).

Surveillance during transition period (1990 to 1993)

National programme to fight Brucellosis in animals and humans

The MoA and MoH had jointly elaborated a programme in 1990, including inputs from the Ministries of Finance, of National Development and of Trade & Industry, to reduce the incidence of brucellosis by encouraging cooperation between the medical and veterinary sectors and using modern technologies and science (*Enkhbaatar L et al, 2004*). In 1991 a national programme for 1992 to 1995 for human and animal was implemented (*Ministry of Agriculture et al, 1991*). This programme included T&S, vaccination, hygienic and management methods training of veterinarians and medical staff, and improved treatment of patients (*Ministry of Agriculture et al, 1991*) (*Ministry of Agriculture et al, 1992a*) (*Ministry of Agriculture et al, 1992b*) (*Ministry of Agriculture et al, 1992c*). It also planned to test all female animals (cattle, sheep & goats) in Aimags and Soums (*Enkhbaatar L et al, 2004*).

Restructuring the economy

However, due to lack of funds, this programme was not implemented as foreseen (*Ministry of Agriculture, 1976*): with the collapse of the former Soviet Union in 1989, Mongolia had suddenly lost its traditional source of economic assistance and traditional external trading partners, the Council for Mutual Economic Assistance (COMECON). Until then, the assistance from the former Soviet Union had amounted to 30% of GDP. This marked the beginning of the transition era for the Mongolian economy from centrally planned to market oriented. Cornerstones of this transition process were the privatisation in agriculture, livestock, industry and services such as health services or veterinary services. Thus there were two difficulties, (i) the impact of the external shock and (ii) the internal economic transition, which had major consequences on the economy and social situation: GDP dropped by about 20% between 1990 and 1993, and unemployment reached 20% (*World Bank, 1997b*). The State took rigorous austerity measures to stabilise its budget and public

expenditures declined from 52% of GDP in 1990 to 28% in 1993, all this against a background of declining GDP (*World Bank, 1997b*).

From 1991 onwards, the Government introduced a series of structural reforms to liberalise the economy which included the privatisation of livestock. By the end of 1992, 18 out of 25 million livestock had been privatised (*World Bank, 1997b*). The Government's budget shrunk to match the Government's reduced market role. The Government focused on its core business and improved the efficiency of service delivery. This restructuring process affected the public health and livestock sector as well. Public health expenditures declined from 5.5% of GDP in 1991 to 4.0% in 1993, producing unfortunate impacts on health indicators such as maternal mortality and infant mortality (*World Bank, 1997a*). On the other hand, Veterinary Services had been relatively unscathed as restructuring had been done for the time being on the level of central directorate and laboratory, but not in field services (*Honhold N., 1994a*). Preventive disease measures were still a major focus of veterinary interventions, and vaccinations were still provided free of charge -- except for a small nominal injection fees. The privatisation process however split the herds among a large number of herders. This meant that the area the vets had to cover was ten times larger than that covered prior to the transition period; this created a lack of veterinary services (*Honhold N., 1994a*). The resulting ratio, one veterinarian to 70 herders, was low given the terrain and the nomadic livestock breeding. Additionally, the livestock numbers have increased with 34.5% from 1989 to 1998⁵². The reasons for this were the privatisation, an increase in herders, social insecurity (*Honhold N., 1994a*) and a reduced market for animal products, reflected by meat processing plants working at 20% capacity by the end of the 1990s.

Impact of transition on Brucellosis

⁵² (*State Statistical Office of Mongolia, 1999*)

Number of cattle in 1989: 2'692'700; in 1998: 3'725'800; increase: 38%

Number of sheep in 1989: 14'265'200; in 1998: 14'694'200; increase: 3%

Number of goats in 1989: 4'959'100; in 1998: 11'061'900; increase: 123% (because value of cashmere wool)

Several aspects favoured the further spread of brucellosis during the market transition period. They can be subsumed under the failure of hygienic measures and poor prevention. During privatisation of the livestock infected and uninfected herds had been mixed. Animal movement was no longer under veterinary control and there was no longer any identification system (tagging) in place for any livestock species (*Garin-Bastuji B., 1999*). The animals had been distributed irrespective of whether people knew anything about livestock (*Jefferies I., 1996*). Dairy products delivered to consumers in urban areas, industrially pasteurised in the centrally planned economy, had been delivered directly to the consumers without pasteurisation during the transition period (*Veterinary state general supervisor, 1992*). On the human side, the Public Health services were no longer able to investigate brucellosis infection and to provide early diagnosis (*Ministry of Agriculture, 1976*). The costs for the treatment of brucellosis grew rapidly.

Surveillance during post-transition period (1994 to 1999)

Combined policy with Test and Slaughter and vaccination

In 1997, Mongolia joined the WTO, as the first country in transition outside Eastern Europe (*World Bank, 1997a*). The elimination of brucellosis was an important condition to access free foreign markets. "... the most cattle in Mongolia have brucellosis resulting in Russian's refusal on meat imports from Mongolia" (*bizMongolia, 2002*). As a member of WTO, Mongolia had to follow international standards of hygiene and safety and to ensure registration, monitoring and prevention from zoonotic diseases. With increasing international trade the movements of animals and animal products had augmented the exposure of animals and humans to infectious diseases (zoonoses). As a result, a new programme was decided to fight brucellosis in human and animals between 1996 and 2000 (*Ministry of Food and Agriculture, 1996*). It was a combined policy between slaughtering infected animals and providing vaccines for healthy animals after testing.

Factors hindering Test and Slaughter

However, privatisation and inflation had adverse effects on this combined policy (*Enkhbaatar L et al, 2004*), because it required accurate animal identification, herder cooperation and an expensive compensation scheme for slaughtered animals. Furthermore, slaughtering of positives was voluntary, and nearly a third of the identified infected animals were left in their flocks, (*Khohoo A. et al, 1995*). Privatisation of Veterinary Services had increased in 1999, despite concerns about the ability of the Mongolian economy to support an adequate supply of private veterinary services. This had threatened the sustainability of veterinary services, especially in the rural areas (*Garin-Bastuji B., 1999*). As consequence most of the laboratories in rural areas closed down. But testing was an important factor in the strategy applied and timely response of case information by laboratories was crucial. Additionally, quality problems occurred; for instance, the locally produced antigens used for brucellosis testing (RBT, CFT, SAT and MRT analysis) did not fulfil the O.I.E. international requirements, even when officially tested by the Mongolian Veterinary Quality and Control Laboratory (VQCL) (*Garin-Bastuji B., 1999*). The latter was compounded by the reality that approximately every fifth infected cattle does not show antibodies in its serum until after abortion (*Honhold N., 1994b*).

Moving away from Test and Slaughter

The understanding was that in Mongolian context a strategy based at least in part on a T&S approach could very unlikely be able to control brucellosis to a significant low level and to prevent the further increase of human incidence (*Garin-Bastuji B., 1999*). The prevalence in the infected herds had been estimated to be too high. Socio-economic changes such as privatisation of the livestock and increasing herd size, the nomadic structure of ownership, privatisation of veterinary services and poor laboratory infrastructure were unfavourable factors to such an approach. It had therefore been considered to change the strategy and turn back towards a whole herd vaccination strategy (*Garin-Bastuji B., 1999*). It was the only feasible approach to brucellosis control during this period in Mongolia.

Recent surveillance strategy after 1999 and implementing of whole herd vaccination strategy

National programme on “Animals Health”

With the aim to protect livestock animals from zoonotic diseases the Mongolian Government approved, in 1999, the national programme on “Animals’ Health” (*Ministry of Agriculture, 1999*), to improve the quality of veterinary services, prevent enormous socio-economic losses and increase the export rate of animal products. Brucellosis was included in this “Animal’s Health National Programme” among other diseases such as TB, leucosis, glanders, infectious anaemia of horses, foot & mouth and plague. The programme is supposed to eliminate brucellosis from Mongolia by year 2010. The MoA was charged to conduct surveillance of brucellosis in animals and to elaborate mid and long term projects on prevention. Based on this, the MoA has ordered monitoring testes to investigate the prevalence of brucellosis in camels, cattle, sheep and goats (*Ministry of Agriculture, 2000c*). The screening involved 793,600 animals all over the country, and showed an average brucellosis infection rate of 1%. But the spread was very unequally dispersed over the single Soums and reached peaks of 21.9% (*State Veterinary & Animal Breeding Department of the Ministry for Food & Agriculture et al, 2001*). The high rate of a quarter of all identified infected animals had not been slaughtered but had remained with the herders.

Whole herd vaccination campaign

Based on these data, the MoA implemented in 2001 (*Ministry of Agriculture, 2001*) a whole herd vaccination plan calling for (*Mikolon A.B., 2000*) (*State Veterinary & Animal Breeding Department of the Ministry for Food & Agriculture et al, 2001*): (i) 10 years yearly vaccination of the new born female kids and lambs with Rev.1, and calves with S19; (ii) the vaccination of all breeding adult females cattle within 3 years (with S19), sheep and goats (with Rev.1), and repeat of this vaccination 3 years later; (iii) the assessment of the vaccination success through a survey before

repeating vaccinations; (iv) the marking of all vaccinated animals (ear tag); (v) the testing of breeding males twice a year and the slaughtering of reactors; and (vi) the surveillance -- through infection level detection -- of herders and other risk groups. Thus, it was planned to vaccinate 5.3 million animals in 11 Aimags that same year. The vaccination coverage could be realised with 86% to 95% (*Ministry of Agriculture, 1999*).

National Programme to Control Communicable Diseases

From the human side, the fight against brucellosis has been put into a wider context: The “National Programme to Control Communicable Diseases” declaring in 2002 to decrease communicable diseases and mortality, focused in one of its sub programmes on infectious diseases with natural foci and zoonosis (*Prime Minister of Mongolia et al, 2002*). The following measures were foreseen to fight brucellosis; (i) education and dissemination on brucellosis prevention methods; (ii) improvement of brucellosis surveillance on an intersectoral level and (iii) the improvement of intersectoral collaboration and participation.

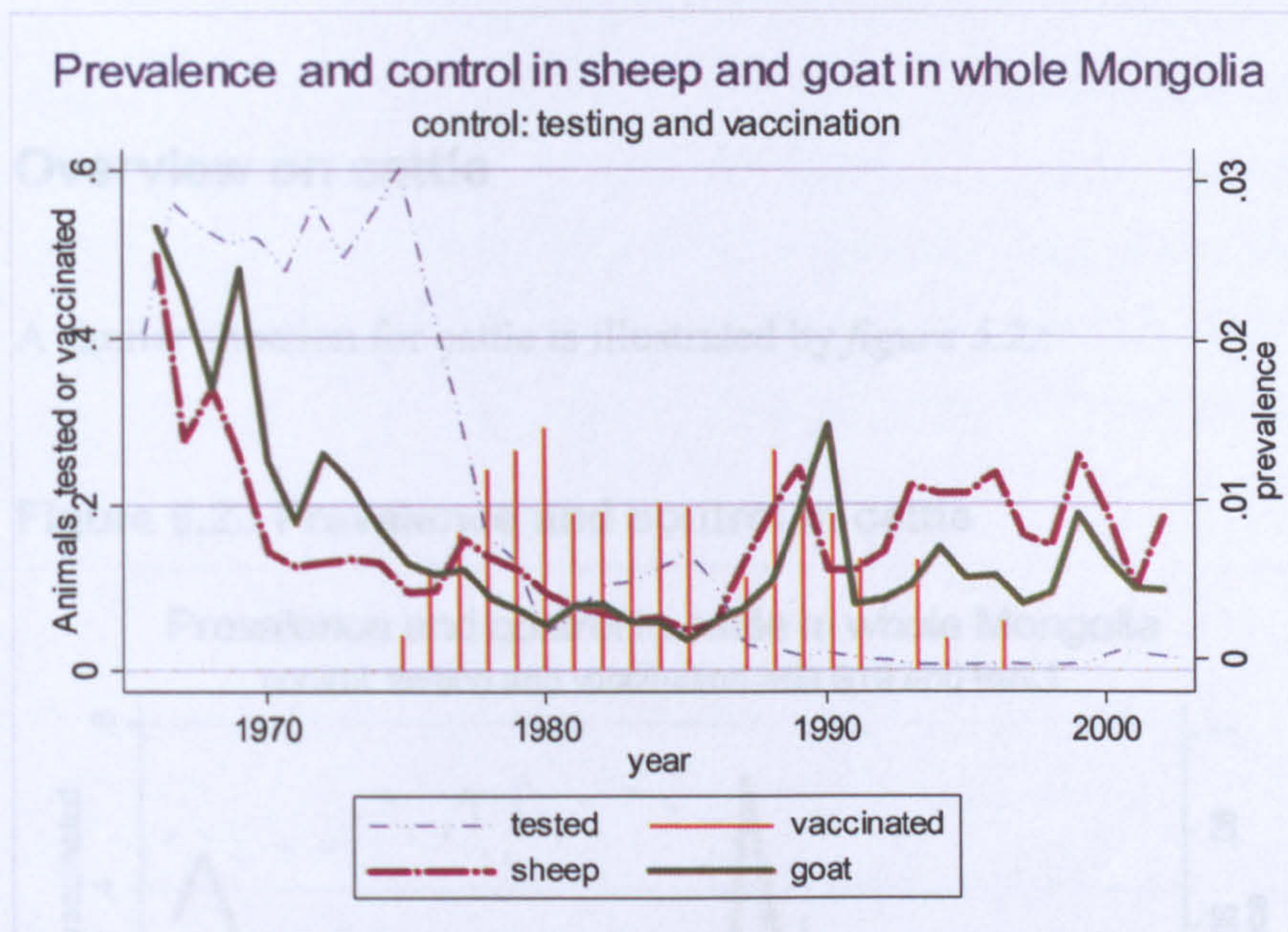
3. Reviewing policy with quantitative data

The review of the governmental policy papers and grey literature has given an insight to the different elements, stages and causes of the policies applied. However the policy papers were on intention or plans. No progress reports of implementation activities were available, uncertainty therefore remained as to the real nature of surveillance activities. Only one Governmental order insisted on the implementation of a previous order, because its implementation has been judged as poor (*Ministry of Health, 1979*). Data collection on testing and vaccination allowed screening the current policy implementation with quantitative data and to illustrate this with graphs.

Overview on small ruminants

In *figure 5.1.* brucellosis prevalence in sheep and goats is compared to testing and vaccination for the time period 1966 to 2002. The figure shows average data: all Aimags are put together and give a country-wide aggregate.

Figure 5.1.: Prevalence and control in small ruminants



Derived from material collected for this thesis

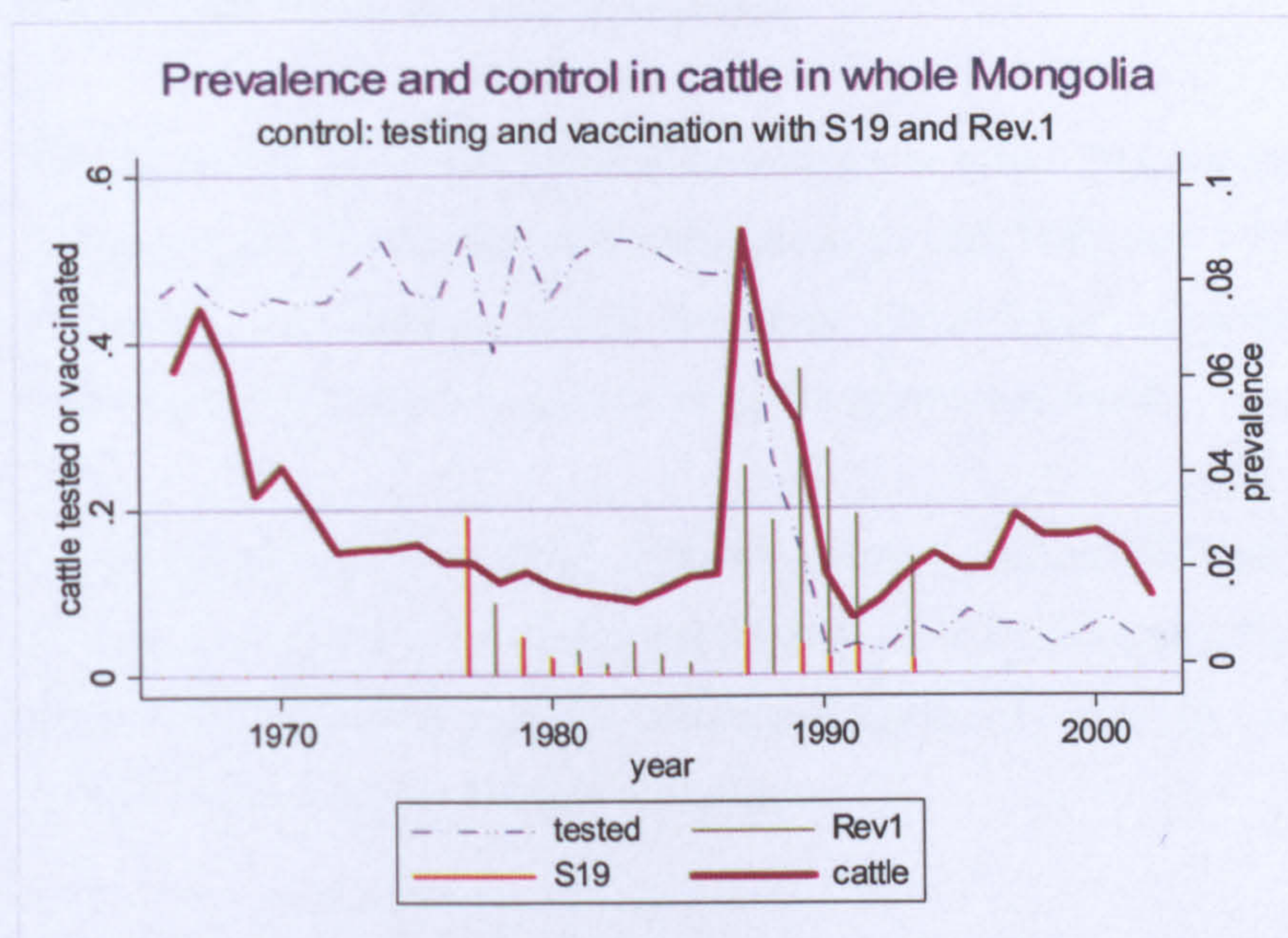
From this rough overview, the following stages can be made out: vaccination in SR began in 1975, after a considerable prevalence decline, from 2.5% in mid 1960s up to less than 1% from the mid 1970s onwards. As soon as vaccination started, the percentage of animals tested dropped from nearly 60% to about 10%. The average vaccination coverage increased over the years up to about 30% in 1980, and levelled out at about 20% in 1985. During the same period of time, the prevalence dropped constantly to less than 1%. However, after 1985 the vaccination coverage, as well as the prevalence rate (around nearly 1%), became quite volatile. The whole SR flock vaccination campaign 1975 to 1985 is well reflected by *figure 5.1.* and it shows how the prevalence in sheep and goats was at its lowest level in 1985, after 11 years of vaccination. However, the prevalence started to increase in 1986, the same year vac-

inations stopped. The prevalence continued to increase until the vaccination coverage increased between 1988 and 1991; following this, only sporadic vaccination took place. We have seen, that the policies could not be implemented in early 1990s because of lack of funds, and in later 1990s privatisation and inflation had adverse effects on the implementation of the planned policies. During this time, prevalence levels become incoherent; it can be supposed that data collection was inconsistent and irregular in the 1990s.

Overview on cattle

A similar situation for cattle is illustrated by *figure 5.2.*:

Figure 5.2.: Prevalence and control in cattle

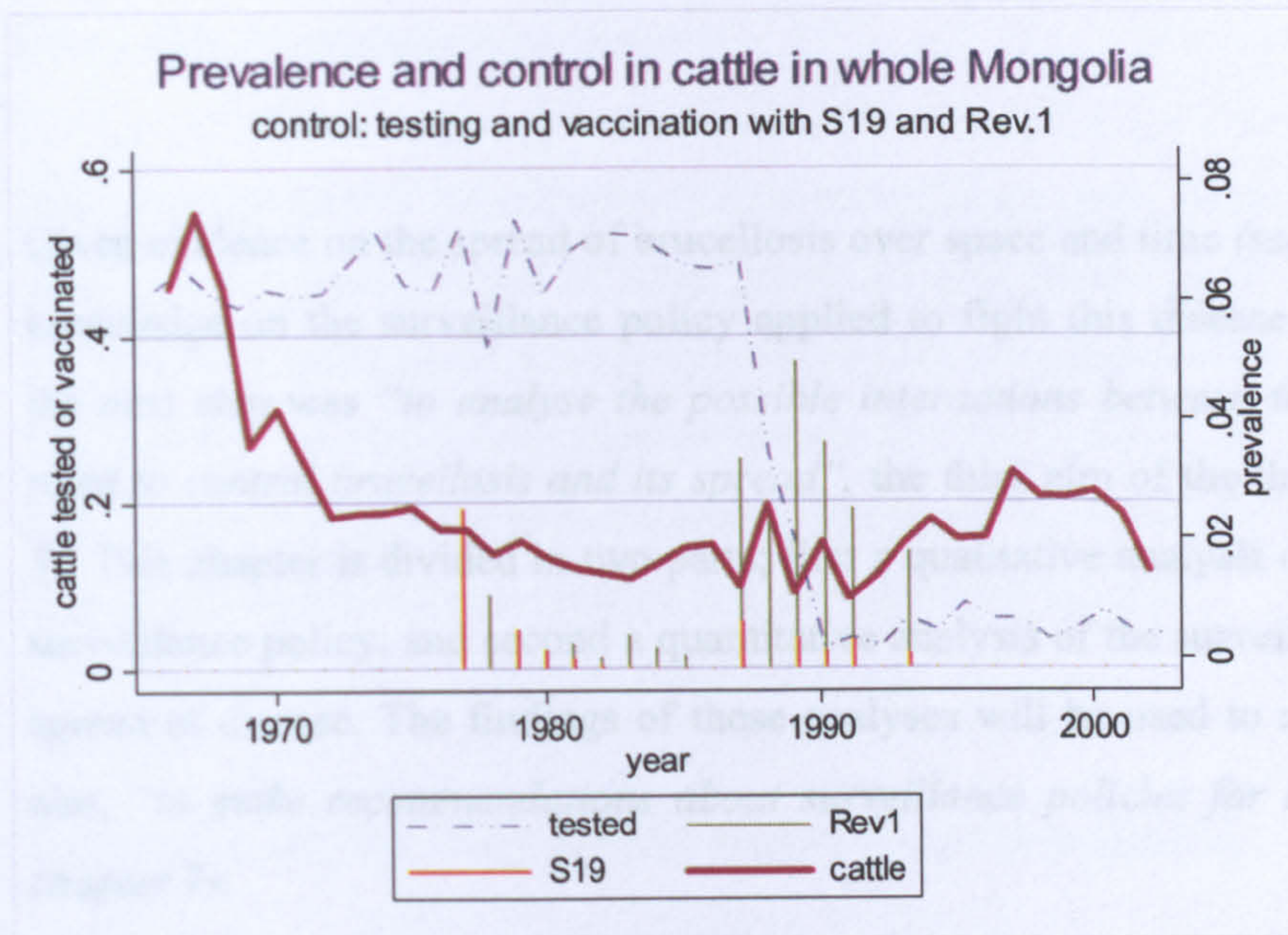


Derived from material collected for this thesis

The prevalence rate declined from above 6% in the mid 1960s to about 2% in early 1970, and stayed there up until 1986. A little fewer than 10% of the cattle had been vaccinated, from 1976 to 1985, with S19 and Rev.1, confirming that the whole herd vaccination was in SR flocks and actually not in cattle. During the same time, the

percentage of animals tested was more or less constant (about 50%). Then, matching with the review on the policy papers, the whole picture suddenly completely changed in 1987 as the testing had been reduced to very low levels, vaccination coverage had risen to a level of around 20%, occasionally reaching 40%, and the prevalence rate rose fourfold to over 8%. The vaccination campaign in cattle (using mostly Rev.1) lasted until 1991, and completely stopped after 1993. During the period of more intense vaccination the prevalence rate dropped slowly to a level of around 2%. This figure shows how the data have to be interpreted carefully: it can be supposed, that the prevalence showed for the time period before 1987 contained reported data. However, as elaborated in chapter 4, it seemed to be obvious that from 1987 onwards, the reported prevalence might have been mixed with data from surveys. This is likely because it can be assumed that vaccination campaigns were accompanied by surveys, at least during the first years of the campaign.

Figure 5.3: Control in cattle, and prevalence in cattle without Aimags with vaccination



Derived from material collected for this thesis

The figure 5.3. shows the level of prevalence in cattle after having taken out those Aimags where vaccination had taken place in year 1987 and 1988. The course of prevalence rate remained within the range 1% to 2%, confirming the analysis in chapter 4 on the influence of surveys on the prevalence stated.

This historical overview of the different policy strategies will lead us, together with the overview of the epidemiological patterns, to the third aim: *"To analyse the possible interactions between the strategies applied to control brucellosis and its spread"*. This will be treated in next chapter 6.

Given evidence on the spread of brucellosis over space and time (*see chapter 4*), and knowledge on the surveillance policy applied to fight this disease (*see chapter 5*), the next step was “*to analyse the possible interactions between the strategies applied to control brucellosis and its spread*”, the third aim of the thesis (*see chapter 3*). This chapter is divided in two parts; first a qualitative analysis of the Mongolian surveillance policy; and second a quantitative analysis of the surveillance policy and spread of disease. The findings of these analyses will be used to address its fourth aim, “*to make recommendations about surveillance policies for brucellosis*” (*see chapter 7*).

1. Qualitative analysis

In the current section, we assess the Mongolian policy for brucellosis control against the basic steps required for an epidemiological surveillance system, according to best practice. All governmental policy papers have been included in this analysis, despite different levels of completion, and included resolutions, orders, guidelines, methodology papers, project plans, reports or minutes of Cabinet meetings. The detailed analysis is presented in *appendix 6.1.*; results only are presented here.

Basic elements of surveillance

Epidemiological surveillance entails the use of epidemiology and continuous systematic surveys, analyses and interpretations of health-related data (*Krämer A. et al, 2003*). The purpose is the determination of needs for immediate or longer range actions in response to diseases. Changes in the occurrence of diseases and the risk fac-

tors of contagious diseases are tracked to estimate future risks of infection, environmental or behavioural. Epidemiological surveillance is the basis of an evidence based fight against infectious disease.

The development of an epidemiological surveillance cycle requires the following consecutive steps (*Krämer A. et al, 2003*) (*Teusch Steven M. et al, 2000*): (i) the objectives of the surveillance system; (ii) the set of case definitions; (iii) the methodology and mechanisms of data collection; (iv) the tools for data analysis and interpretation; (v) the dissemination of results; (vi) the implementation and finally (vii) the regular evaluation to ensure the defined objectives are met.

Analysis of the Mongolian surveillance policies

(i) Definition of the objectives

The first step in the establishment of a surveillance system is the definition of strategic objectives and the intervention programme to meet these objectives. The three main general strategies against a disease condition are *control*, *eradication* and *prevention*.

A *control programme* includes measures to reduce the frequency of an illness already present in a population. The aim is to reduce the impact and frequency of this disease on the health status of a population. The organism will not be eliminated completely but an acceptable level of infection will remain. Thus the control programmes will continue indefinitely.

Eradication is conceptually different from control and is achieved by different measures. An *eradication programme* aims to eliminate a species of infectious organism from a territory. If limited to an area, the term “regional elimination” is used, as there is the risk of reintroduction of the pathogen from other geographical areas, thus continuing need for control measures (*Dowdle W R et al, 1997*). New outbreaks are due to the importation of the disease from infected territories. Therefore quarantine

of imported animals can prevent disease introduction. Introduction of disease can be controlled by isolation and slaughter of diseased and exposed animals. For humans none of these measures are applicable. Therefore the objective of eradication of a disease in human is the global elimination of the occurrence of this given disease.

Preventive measures aim to exclude an infectious organism from a geographical area in which it is absent or to protect a population from a disease that already occurs in its geographical area. These three main strategies can form an overall strategy, beginning with control programmes, then changing to eradication and ultimately moving to prevention of the reintroduction of the disease. Unless accurate and current epidemiological information is available, the decision-making by those charged with policy making is likely to be intuitive.

Definition of objectives for brucellosis surveillance

The definition depends on many factors, such as (i) the prevalence in herds and flocks; (ii) the type of husbandry; (iii) available economic resources; (iii) impact on public health and (iv) potential international trade implications (*Robinson A, 2003a*).

Mongolian policy analysis

The analysis showed that the Mongolian policy papers have defined the objectives as *control, eradication* or *prevention*. The related intervention programmes were described as *T&S, vaccination* and *implementation of hygienic management practices*. The majority of the stated strategic objectives aimed at preventing the further spread of the disease. The vaccination campaigns however, in the 1970s in SR, in the 1980s in cattle and currently SR and cattle, aimed at eradicating brucellosis.

(ii) Case definition

Of crucial importance for any epidemiological surveillance system is a clear case definition, defining which appearance of a disease is under surveillance (*Teusch Steven M. et al, 2000*). The degree of certainty regarding diagnosis should be categorised as “suspected” or “confirmed. The case definition should assure the application

of a congruent standard over time and space. But as knowledge of a disease and its associated laboratory testing improves over time, alterations in case definitions often lead to changes in sensitivity and specificity. These changes must be taken into account in analysis and interpretation of trends.

Case definition in brucellosis surveillance

WHO recommends the following case definition for brucellosis in humans (cited out of (WHO, 1999)):

"Clinical description:	An illness characterized by acute or insidious onset, with continued, intermittent or irregular fever of variable duration, profuse sweating particularly at night, fatigue, anorexia, weight loss, headache, arthralgia and generalized aching. Local infection of various organs may occur.
Laboratory criteria for diagnosis:	<ul style="list-style-type: none">• Isolation of <i>Brucella spp.</i> From clinical specimen or• Brucella agglutination titre (e.g., standard tube agglutination tests: SAT>160) in one or more serum specimens obtained after onset of symptoms or• ELISA (IgA, IgG, IgM), 2-mercaptoethanol test, complement fixation test, Coombs, fluorescent antibody test (FAT), and radioimmunoassay for detecting antilipopolysaccharide antibodies; and counterimmunoelectrophoresis (CIEP).
<u>Case classification</u>	
<i>Suspected:</i>	A case that is compatible with the clinical description and is epidemiologically linked to suspected or confirmed animal cases or contaminated animal products.
<i>Probable:</i>	A suspected case that has a positive Rose Bengal test.
<i>Confirmed:</i>	A suspected or probable case that is laboratory-confirmed."

So for humans a specific set of symptoms, together with laboratory tests, are needed to describe possible, probable and confirmed cases. However, this definition may require modification depending on the availability of medical and laboratory resources.

With animals, isolation of *Brucella spp.* is used, with or without serological evidence (Robinson A, 2003a). With this it must be possible to categorise animals as *positive, negative* and *uncertain*. Abortion is an unreliable case definition as it can be multi-causal. Brucellosis is a herd or regional epidemiological problem rather than an individual animal problem. Therefore group data are a more accurate measurement of progress.

Mongolian policy analysis

A case definition was mentioned for animals in 1964, and again in 1976, but without yielding concrete guidelines. In fact, case definition was only in policy papers concerning the vaccination campaign of the late 1980s, when methodology was described for testing as well as the epidemiological entity (dairy cattle farm). The current whole herd vaccination campaign represented an element of uncertainty as far as case definition was concerned, because cross-reactions of the attenuated vaccines with live cells of *Brucella* interfere with the testing results.

For humans no case definition was included in the policy papers. Nevertheless, from interviews with key persons it was clear that the WHO laboratory confirmation case definition is currently applied in Mongolia (personal communications with Dr. Tserendolger, director Soum Hospital in Khutgul, and Dr. Baigal, Clinic for Brucellosis, Central Aimag Hospital in Moron) (Roth F., 2003a)). But only Aimag central hospitals were able to diagnose brucellosis by serology, and if the necessary laboratory kits were available (personal communication with Dr. Narantsetseg, general epidemiologist in the Public Health Organisation of Khuvsgul Aimag (Roth F., 2003a)). Because of the long distances from remote areas to the Aimag centres, most patients infected with *Brucella* remained non laboratory confirmed cases. This confirmed the speculation of under-reporting of brucellosis incidence, emanating from the extremely high contamination rates reported by various surveys (see chapter 4).

The applied case definition did not consider the actual situation as access to serological confirmation of brucellosis was very limited. There were further indications confirming the assumption of under-reporting of human brucellosis: (i) various sur-

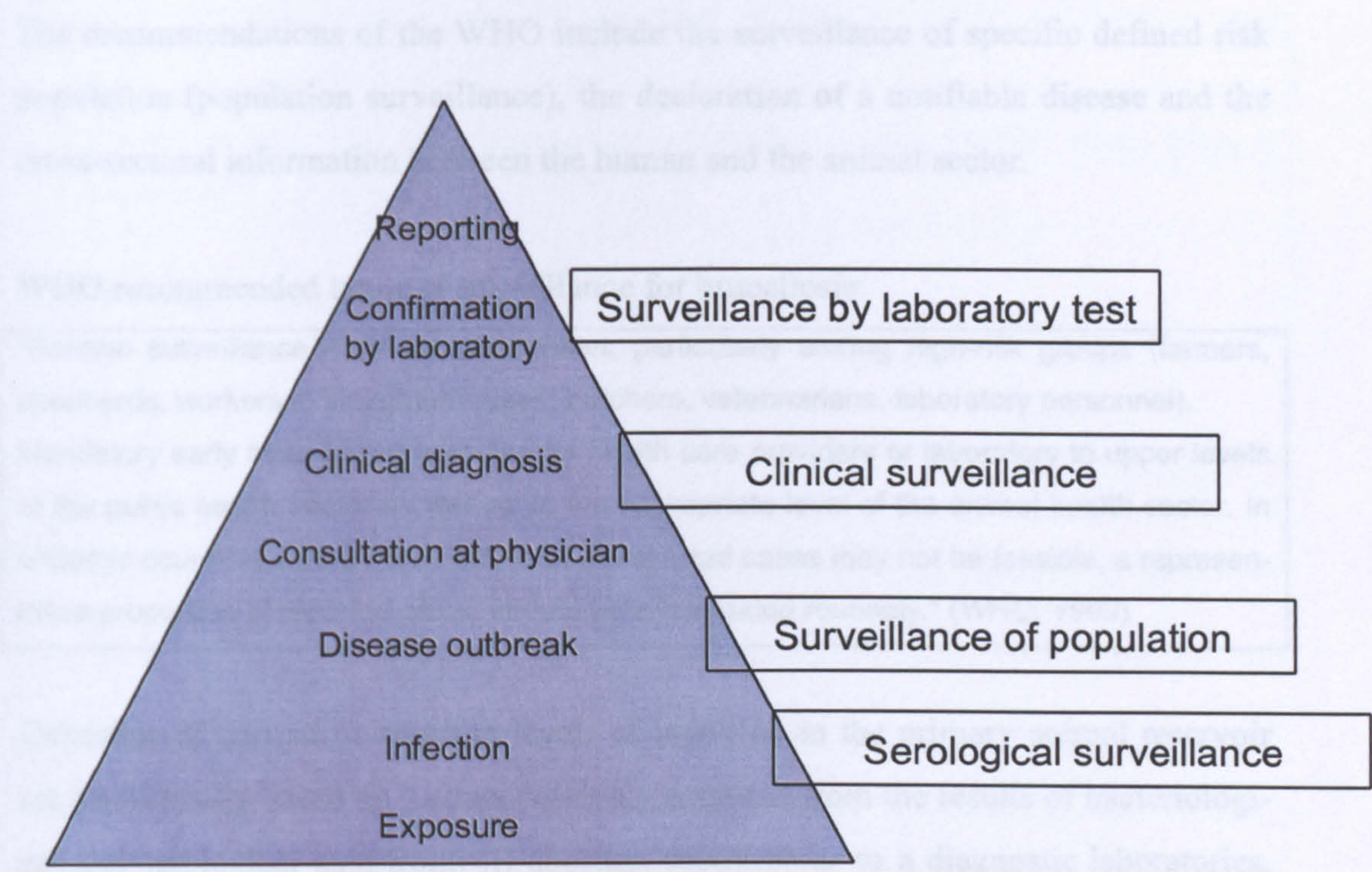
veys reported extremely high contamination among risk groups, which is however not represented in the reported incidence rates (see chapter 4); (ii) most of the patients treated for brucellosis suffered from the chronic form of disease, reflecting late diagnosis and poor access to diagnosis (*see chapter 4*); (iii) the reporting of human cases to the central authorities, which compile the data on human incidence, is weak (see further down : 61.6% of the physicians were not aware that they should report brucellosis cases (*Badarch ULAMBAYAR, 2001*), and personal communication with Dr. Narantsetseg, general epidemiologist in Public Health Organisation of Khuvsgul Aimag (*Roth F., 2003a*)), confirmed that Soum authorities often do not send their files to Moron, the Aimag Centre.

This is strong evidence for the reported brucellosis incidence in humans being far below the current level of contamination. This is problematic as it meant that only a small fraction of the infected population was treated. In addition, the past under-reporting hinders the monitoring of current and future surveillance activities, as an increase of reported human cases does not necessarily mean a current increase in contamination, but could mean an improvement in diagnosis and reporting.

(iii) Data collection

The different procedures or mechanism in data collection follow different objectives and are applied in different circumstances. Common to all is that they can only grasp a part of the real infections of populations. That means that under-reporting of the true infection rate is always the case. This fact is described as the *iceberg principle of surveillance of infectious diseases*, illustrated by *figure 6.1*. (*Krämer A. et al, 2003*).

Figure 6.1.: The iceberg principle of surveillance of infectious diseases



Source: (Krämer A. et al, 2003)

The dynamics of infections in populations involves different levels, which have to be approached by different strategies of data collection. It is obvious that with disease reporting only the top of the iceberg is concerned. The confirmation by laboratory test is very specific, as only clinically diagnosed cases are followed by laboratory tests, whereas not all clinically diagnosed cases are examined by laboratory tests. Thus, a surveillance system considering clinically diagnosed cases would be more sensitive but less specific. A population survey gives information on the disease outbreak rate within a population, but since not all infected persons have signs of disease, serological surveillance provides the final stage of information on the infection rate within a population.

Data collection in brucellosis surveillance

The recommendations of the WHO include the surveillance of specific defined risk population (population surveillance), the declaration of a notifiable disease and the cross-sectoral information between the human and the animal sector.

WHO recommended types of surveillance for brucellosis:

"Routine surveillance must be undertaken, particularly among high-risk groups (farmers, shepherds, workers in slaughterhouses, butchers, veterinarians, laboratory personnel). Mandatory early case-based reporting by health care providers or laboratory to upper levels of the public health sector as well as to the appropriate level of the animal health sector. In endemic countries where investigation of all reported cases may not be feasible, a representative proportion of reported cases should be investigated routinely." (WHO, 1999)

Estimates of current or baseline levels of infection in the primary animal reservoir are traditionally based on "...data passively acquired from the results of bacteriological and serological data from: (i) abortion submissions to a diagnostic laboratories, (ii) routine testing of on-farm samples, such as milk or blood, (iii) notifications from veterinarians if brucellosis is reportable to the authorities, and (iv) off-farm sampling from markets or slaughterhouses." (Robinson A, 2003a). As these results may be biased, active surveillance should be undertaken to provide more reliable estimates. This can best be done by a random sampling programme (Robinson A, 2003a).

Intersectoral collaboration at this stage is appropriate, as surveillance data on human brucellosis can be a sensitive indicator of the status of animal infection, therefore human epidemics may direct veterinary epidemiologists to foci on animal infections. "Animal brucellosis, especially when caused by *B. melitensis*, can often be identified through investigations of cases in humans. So cooperation with public health authorities is important" (Corbel M. et al, 2000).

Often, existing data sets such as administrative systems, risk-factor surveys, health interviews, can provide surveillance data. The recommendation of the WHO for minimum data elements defines three levels (cited out of:(WHO, 1999)):

"Case-based data for investigation and reporting

- Case classification
- Unique identifier, age, sex, geographical information, occupation and ethnic group if appropriate

Date of clinical onset, date of reporting

- Exposure history
- Outcome

Aggregated data

- Number of cases by case classification (probable / confirmed), age, sex, geographical area, occupation"

Data on the animal sector are of further interest for the human sector too and should therefore include the following: (i) data from census in livestock and human, whereas on the animal side the unit of interest is both the individual animal and the herd; (ii) activities performed such as vaccinations, blood samplings, etc., and the recorded results such as vaccinations given, number tested, number positives/negatives; (iii) animal movements; (iv) geographical data.

Mongolian policy analysis

Most policy papers have described the data collection methods in considerable detail according to the requirements described above. Nevertheless, uncertainty of the estimates remained due to mixing of the reported data with the data gained from surveys (*see chapters 4.3. and 5.3.*).

(iv) Data analysis

An integral part of a surveillance system is the determination of the appropriate analytical approach. For most conditions an assessment of the number of cases or rates is followed by a description of the population, place, time and the period over which the condition occurs. Therefore, the first step in the conversion of the data into information is a descriptive analysis on population, place and time. Explorative data

analyses involve techniques to make the overall dataset more understandable. Visualisation can be made with charts. The analyses of epidemiological data by means of various factors over groups of persons may lead to the identification of risk groups. An important procedure in this step is the validation of data, where it is assessed if the data are congruent and consistent. This can be performed through automatic procedures, through expertise and existing knowledge.

Data analysis for brucellosis surveillance

WHO recommends graphs, tables and maps with distinguished case classification:

“Graphs:	Number of probable / confirmed cases by month.
Tables:	Number of probable / confirmed cases by age, sex, month, place.
Maps:	Number of probable / confirmed cases by place.”(WHO, 1999)

Indicators, defined as “.....a synthetic bit of information able to describe both state and dynamic of a particular aspect of the system studied” (*Giovannini A. et al, 1 A.D.*), could give further useful information for surveillance. Specific indicators of brucellosis surveillance can be identified as the percent variation of incidence in humans and prevalence in animals by territorial and time unit, or the change of herd incidence. But it is important to know and describe the inherent limitations of the data.

Mongolian policy analysis

Data analysis is completely missing in all policy papers reviewed. The only exception was 1988, where a methodology paper planned to study infected cattle data. This lack of analytical approach has also been noted during the review of Mongolian scientific literature, which included very little analyses (*see chapter 4*). It seemed that this was the weak spot of the epidemiological surveillance policy. Policy makers usually had to implement new surveillance activities without having data analysis and evaluation reports of the previous surveillance activities.

(v) Dissemination

Technical reports on health conditions, activities performed and progress aim decision-making authorities and should be presented accurately that the implications of the information can be clearly seen by central policy makers and field operators. So the surveillance should guide the initiatives for control, eradication or prevention to those who need to take action (*WHO, 2001*).

Dissemination of results in brucellosis surveillance

WHO recommended the following principal uses of data for decision-making:

"Surveillance data

- Estimate the magnitude of the problem in humans and animals
- Monitor the distribution of the diseases in humans and animals
- Monitor and evaluate impact of prevention activities in humans, and of control / elimination measures in animals

Investigation data

- Identify populations at risk
- Identify potentially contaminated products of animal origin
- Identify potentially infected animals sources (herds or flocks)"(*WHO, 1999*)

Mongolian policy analysis

Many of the Mongolian policy papers have included these requirements, insofar as the results of the surveys are collected from the Aimags and reported to the central and local authorities. Sometimes, intersectoral information exchange activities have been promoted at conferences, meetings, seminars or workshops.

(vi) Implementation

A surveillance system should ensure activities are planned, implemented, directed to the objectives defined, and be based on evidence. The implementation plan should include (i) methodology (surveillance activities needed), (ii) governance (responsibilities, structures, cooperation, organisation and dataflow), (iii) resources (human, equipment, financial and logistic supports) and (iv) scheduling.

Implementation of brucellosis surveillance

The FAO Guidelines for coordinated human and animal brucellosis surveillance (*Robinson A, 2003a*) stress the importance of political and legal factors in brucellosis surveillance. Strong political support is needed to avoid the under-funding of programmes. Laws have to be enforced for the identification or compensation of infected animals. The FAO Guideline suggests the surveillance activities should be administratively separated from other control activities within government veterinary services to ensure surveillance information in an unbiased format. Other important factors to consider in surveillance are culture, motivation and education. Social pressures may discourage reporting brucellosis infected animals. Educational efforts have to be established and positive motivation could be achieved by a reward system giving incentives for being involved in surveillance activities.

Mongolian policy analysis

The Mongolian policy has met these requirements, as the methodology for fighting brucellosis, such as T&S, vaccination, hygienic methods and management practices were described. However, the concrete implementation of the measures reveal some managerial weaknesses threatening the effectiveness of the immunisation campaigns, as reported about the 1975/1985 vaccination campaign (*see chapter 5.2.*) or the 1987/88 cattle vaccination campaigns (*see further down*). Observations made during field work concluded that the current vaccination campaign (which started in 2001) suffered from managerial omissions critical for ensuring the success of the immunisation: (i) The vaccines have been stored within the private veterinarian sector on Soum level from delivery in April/May onwards up to the administration in August/September during the hot season without cooling, and there has been no subsequent quality controls after storage and before administration. (ii) The vaccinated animals have not been marked and there is currently only a self-control requirement placed on the private veterinary sector concerning the vaccination coverage, without the possibility of the inspectors of the Aimag's Veterinary Offices to perform controls. (iii) To monitor the vaccination efficacy serological testing has been foreseen but not implemented.

The “*education campaigns*” seemed to play an important role and are listed in the analysis, separately from other hygiene methods and management practices. These education campaigns played an important role in the 1960s and 1970s, but a less important role in the 1980s, and only a minor role in 1990s. Within a study on the “population knowledge level on brucellosis” a country-wide survey among 650 persons was conducted and attested to poor knowledge on brucellosis (*Badarch ULAMBAYAR, 2001*). Among those questioned were 260 physicians, of which 61.6% were not aware to notify human cases of brucellosis to Central level, 64.4% had wrong knowledge on the endurance of *Brucella* in environmental conditions, 90% wrongly interpreted the skin allergic test (Burne test), and only a few (8%) knew how to treat acute or sub-acute cases of human brucellosis, or how to treat chronic cases (4%). 83.2% of the physicians thought that food borne transmission would be the main route of brucellosis infection to humans, while direct animal contact would only cause 7.2% of the infection, and aerosol transmission 9.6%. In fact, according to an analysis from 1985, food borne transmission caused only between 5.7% and 6.7% of the human infections, and the main route of infection was direct animal contact (between 89.2% and 94.2%), while aerosol transmission was 3.9%. Most of the remaining 400 study participants⁵³ thought that the sources of human brucellosis were cattle, horses and camels, but not sheep and goats, only 55.6% boiled milk, and the general knowledge to prevent humans from brucellosis infection was, according to this study, insufficient.

Currently, the prevention efforts aimed at herders are focused on the health of the animals rather than on human health⁵⁴. The conclusions reached on the occasion of the Brucellosis Conference in UB, in June 2003, concerning the prevention of human brucellosis have, due to lack of funds, not been implemented. Only the animal portion of prevention has been implemented (whole paragraph: personal communi-

⁵³ Profession among these 400 study participants: 24.5% herders, 23.7% workers with animal products, 20% workers with dairy products, 10.7% unemployed;
Education among these 400 study participants: 20% university, 16.25% college, 35.5% high school, 17.75% secondary school, 10.5% primary school.

⁵⁴ Advice was given to wash hands BEFORE helping in lambing, but not to wash hands AFTER helping in lambing.

cation with Dr. Narantuya, General Director of the Public Health Institute, MoH (*Roth F., 2003a*).

There is strong evidence to conclude that there is a need for disseminating more information concerning the prevention of brucellosis in humans. This should be done adequately for the general population, to the risk group (herders, workers with animal products) and to the physicians.

Regulations on governance issues have been provided on a regular basis and have carefully considered the interaction between the MoH and MoA. However, this could well be improved (personal communications with Dr. Altantsetseg, deputy director of Public Health Organisation of Khuvsgul Aimag, and with Dr. Baigal, Clinic for Brucellosis, Central Aimag Hospital in Moron (*Roth F., 2003a*)).

During the period of the planned economy, the allocations of resources were described in detail, and there seemed to be strong political support for brucellosis surveillance, reflected by considerable funding of surveillance activities. After the shift to a market-oriented economy, in the 1990s, such detailed descriptions of resources supply were replaced by instructions to search for “international cooperation and financing” (*Ministry of Food and Agriculture, 1996*).

Legal concerns, affecting compensation rules for animals infected and slaughtered, have never been included in policy papers. Obviously, this was not an issue during the period of planned economy since the animals belonged to the state, but with the privatisation of the herds this topic has become crucial to ensure surveillance work.

(vii) Evaluation

An epidemiological surveillance system should be evaluated regularly to ascertain its utility and relevance to public health. This can be measured and evaluated in quantitative terms by objective criteria such as incidence, prevalence, mortality, productivity losses, and medical costs. Common difficulties in the evaluation of surveil-

lance systems are under-reporting, diagnostic misclassification and no standardised case definition or production of data which are not consistent or comparative.

Evaluation in brucellosis surveillance

An effective brucellosis surveillance programme should fulfil at least three major requirements (*Robinson A, 2003a*): i) *Sensitivity*, detecting high percentage of field events compatible with brucellosis; ii) *Specificity*, providing a definitive diagnosis for a high percentage of brucellosis-compatible field events; and iii) *timeliness*, enabling prompt field responses to situations identified.

Mongolian policy analysis

The Mongolian surveillance policy have usually foreseen the assessment of the spread of disease and described the managerial aspects. Evaluation of surveillance activities such as the application and implementation of the guidelines and measures, the supervision of veterinary specialists, herders, and other people at risk was often carried out. However, the missing data analysis, and the application of a case definition not adapted to the circumstances, as pointed out above, had an impact on the evaluation, as no demonstrable conclusions could be drawn from the reporting system.

Evaluation reports could not be traced. The exceptions were two reports on the work of the Mongolian-Russian expedition in 1987 and 1988 (*Ministry of Agriculture, 1988*). These concluded that the surveillance activities had not been properly implemented. The expedition teams had encountered conditions favourable to the spreading of brucellosis such as: (i) no plans for vaccination of animals; (ii) no systematic policy for preventing brucellosis in humans; (iii) no coordinated implementation of management practices preventing infection; (iv) under-staffed medical and veterinarian sectors; and (v) lack of modern laboratory equipment and technology (*Enkhbaatar L et al, 2004*).

Further indication of improperly implemented policy can be found in the Norinpil article “Do we bother to eradicate brucellosis in sheep and goats or not?” (*Khohoo*

A. et al, 1995). Conditions preventing successful surveillance activities are listed here, such as (i) the lack of effective supervision due to insufficient manpower; (ii) the poor quality of information; (iii) the uncertain quality of vaccines due to over storage and breaking of the cold chain.

The analysis showed that there was a discrepancy between the policy papers indicating the measures to be implemented, and the actual measures implemented. The managerial and organisational deficits lead to poor quality of the control measures with critical effects decisive as consequence about the success or failure of disease eradication.

The surveillance policy indicated that the policy papers regularly considered governance issues between the MoA and MoH, as these were crucial to assure the success of surveillance activities. Nevertheless, the inter-sectoral collaboration between MoA and MoH to fight brucellosis was traditionally difficult (personal communication with Dr. J. Kolar, former WHO expert in Mongolia (*Roth F., 2003a*)), as the need for the MoH to fight the disease in humans was stronger than the need of the MoA to fight the disease in animals. The losses in animals due to brucellosis was not perceived as very important, however, the goal to prevent human infections made the intervention in the animal sector indispensable. It was therefore not surprising that the demand for better inter-sectoral collaboration was expressed by members of the MoH (personal communications with Dr. Altantsetseg, deputy director of Public Health Organisation of Khuvsgul Aimag, and with Dr. Baigal, Clinic for Brucellosis, Central Aimag Hospital in Moron (*Roth F., 2003a*)) and not by members of the MoA.

A multi-sectoral approach analysing the losses due to brucellosis infection in humans and in animals showed that losses in animals were considerable and that strict surveillance would be, also from a monetary point of view, in the interest of the MoA (*Roth F. et al, 2003*).

Summary of Findings

The qualitative analysis has pointed out four potential weaknesses of the surveillance policy:

- (i) The most important was the missing data analysis. This had depressing effect on dissemination and evaluation.
- (ii) The case definition for human brucellosis was not adapted to the circumstances and resulted in under-reporting of human diseases because of lack of access to proper laboratory diagnoses.
- (iii) Education campaigns, necessary part of control programs, were missing in the 1980s and 1990s, and there was strong evidence for poor knowledge on brucellosis.
- (iv) The actual implementation was not satisfactory, threatening the effectiveness of surveillance measures.

These four topics will be addressed in *chapter 7* as basis for formulating recommendations for surveillance policy (fourth aim of this thesis).

2. Quantitative analysis

The discussion in the first part concluded that there were two specific questions, which should be further analysed by quantitative methods: (i) the impact of the immunisation campaign in SR from 1975 to 1985 which has never been analysed, whether with laboratory methods nor with statistical methods. The data collected for this thesis on the epidemiological spread and vaccination process facilitated the application of mathematical modelling to assess the effect of the immunisation process on disease transmission. This could yield important knowledge for defining the vaccination coverage in future immunisation campaigns. (ii) The surveillance policy shifted in the 1980s from fighting brucellosis in SR to fighting brucellosis in cattle, mainly in dairy farms. No etiological evidence could be found justifying this policy

shift. Statistical analysis of the animal – human transmission was possible using the data collected for this thesis.

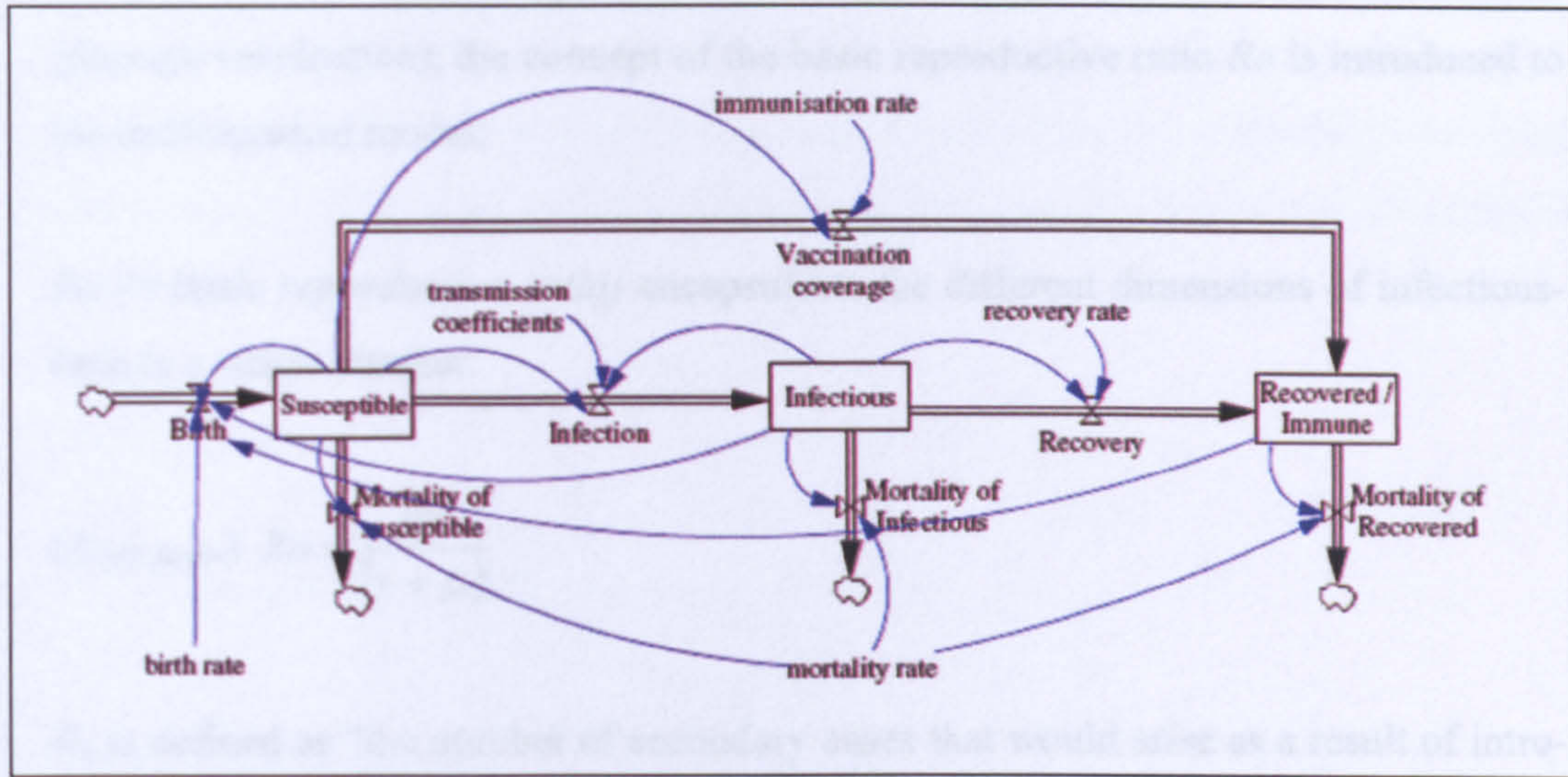
Mathematical analysis on the vaccination campaign 1975 to 1985

SIR Model

The first task was to determine the fraction of the animal population, in the different regions of Mongolia, which should have been vaccinated in order to eliminate brucellosis. The second step was to compare this with the historical data. The transmission of an infectious disease such as brucellosis is a non-linear process governed by the interaction and respective sizes of susceptible and infectious animal and human populations. Vaccination interventions reduce, depending on vaccine efficacy and vaccination coverage, the size of the susceptible population. If the size of the susceptible population drops below a certain threshold, the transmission of the disease can be interrupted. To capture such processes, mathematical models have been developed. The *Kermack-McKenrick Susceptible Infectious Recovered Model* (short: *SIR model*) (see figure 6.2.) is a simple epidemiological model that computes the host – parasite population dynamics of a generalised contagious illness in a closed population over time (Roth F. et al, 2003). This model involves coupled equations relating the number of individuals in the three compartments:

- (i) *Susceptible* $S(t)$,
- (ii) *Infectious* $I(t)$ and
- (iii) *Recovered* $R(t)$ which can also be called *Immune*

Figure 6.2.: The basic SIR Model



An individual moves during the course of natural infection from the susceptible state through the infectious state, and becomes eventually immune. A susceptible individual is removed, if it is vaccinated, artificially to the immune state. The effect this has on the whole population is investigated through the *SIR Model*.

The model has 3 parameters:

- (i) *mortality rate* (μ), assuming constant population size by equal *birth rate* (α),
- (ii) *recovery rate* (γ) and the
- (iii) *transmission coefficient* (β).

Thus the basic equations in this *SIR Model* for the three compartments are:

$$(1_{SIR Model}) \quad \frac{dS}{dt} = \mu(S + I + R) - \mu S - \beta SI$$

$$(2_{SIR Model}) \quad \frac{dI}{dt} = \beta SI - \mu I - \gamma I$$

$$(3_{SIR Model}) \quad \frac{dR}{dt} = \gamma I - \mu R$$

To quantify the relationship between “infectiousness” and “ease of eradication” (through vaccination), the concept of the basic reproductive ratio R_o is introduced to the mathematical model:

R_o (= *basic reproduction ratio*) encapsulates the different dimensions of infectiousness in a single number:

$$(4 \text{ SIR Model}) \quad R_o = \frac{\beta S}{(\gamma + \mu)}$$

R_o is defined as “the number of secondary cases that would arise as a result of introducing one infectious individual into a wholly susceptible population” (McLean A R, 1994). In other words: R_o determines the mean number of individuals infected by contact with a single infected individual before his death or recovery, whereas:

$\frac{1}{(\gamma + \mu)}$ (= *duration of infectiousness*) represents details of the physiology of the

host – parasite interaction,

S (= *total population in the sense of a wholly susceptible population*) the host demography and

β (= *contact rate*) the parasite biology.

The infection is at its equilibrium when it does not spread nor diminish. This is at:

$$R_o = 1$$

A vaccination strategy has to change any aspect of the host – parasite interaction in the matter to bring the effective reproduction ratio (R_e) to less than 1, which will lead to elimination. This can be done by reducing the pool of susceptible population. Through immunisation of the fraction p the number of susceptible becomes:

$$(1-p)S$$

Immunisation p is defined as the vaccination coverage vc times vaccine efficacy ve .

The immunisation level has to be linked with the degree of infectiousness (R_0), which is based on epidemiological and demographic data, to set the target level for eradication. This level p_c , called as the *critical immunisation level for eradication*, is found at

$$(1-p_c)R_0 = 1$$

and can be solved to yield:

$$(5 \text{ SIR Model}) \quad pc = 1 - \frac{1}{R_0}$$

The above conditions show that it is not necessary to vaccinate every individual to achieve elimination. Thus, the critical immunisation level for eradication is of great interest to know the fraction of the population which has to be vaccinated to achieve the goals. However, this model leaves out complexities such as age structure, seasonality, or heterogeneity (McLean A R, 1994) (see discussion in chapter 7).

In real life situations, populations are not closed and may change by reproduction, mortality and transfers. Waves of infectious disease may be partially explained by population dynamics. For example, a population decimated by a highly mortal disease below the threshold of transmission may slowly recover to reach the size allowing an epidemic outbreak of the disease.

The *SIR Model* has already been used as basic underlying model in modelling brucellosis infection on various occasions: Gonzales (González-Guzmán J et al, 1994) has applied this model for the description of the evolution of bovine brucellosis in Chile. Zinsstag (Zinsstag J. et al, 2005a) has modified and extended this model for developing a dynamic model of livestock-to-human brucellosis transmission in Mongolia to assess the future benefits of improving animal health, and hu-

man health through the control of brucellosis by vaccination of livestock (*Roth F. et al, 2003*).

In our data analysis, we applied some of the modifications already introduced to the basic *SIR Model* during the previous work on brucellosis transmission in Mongolia (*Roth F. et al, 2003*) (*Zinsstag J. et al, 2005a*). The modifications as seen in *figure 6.3*. were as the followings:

(i) Brucellosis affects fertility, which has been well thought-out by considering a seroprevalence-dependent effect on the birth rate:

$$\alpha_{\text{(effective)}} = \alpha_{\text{(baseline)}} (1 - (\eta(I/(S + I + R))))$$

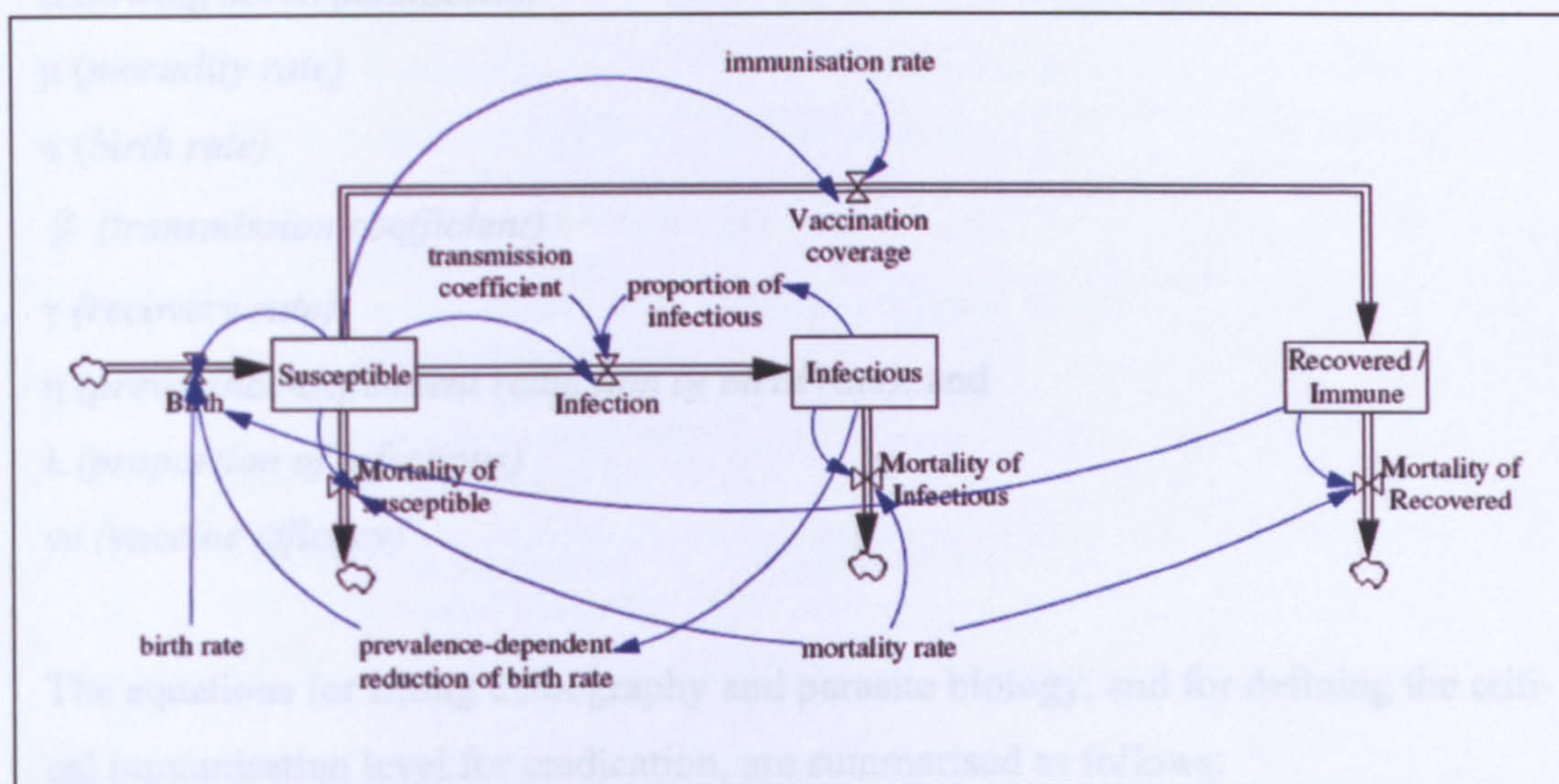
where η is the *prevalence-dependent reduction of birth rate* α , including abortions, among the seropositive animals.

(ii) because only data on seropositive animals are available, only one compartment for the *Seropositive* animals is defined, instead of two for *Infectious* and *Recovered*. In other words, the *recovery rate* or *immunity-loss parameter* γ is put to zero. In the compartment for *Immune* there are only animals immunised through vaccination and none through recovery.

(iii) The new parameter λ is introduced, defining the *proportion of infectious* animals, which are in the stage of infecting other animals. In other words: among the seropositive animals in compartment *Infectious* only a fraction λ is excreting bacteria, and is therefore infectious. Thus, adding this to the formula for *incidence in animals*, the new definition is derived as:

$$\text{incidence} = \lambda\beta SI$$

Figure 6.3.: The Brucellosis SIR Model



This leads to the slight modification of our equations for the three compartments and to the modification of the parameter R_0 *basic reproduction ratio*:

$$(1 \text{ brucel model}) \quad (dS/dt) = (\alpha_{\text{baseline}} (1 - (\eta(I/(S + I + R)))))(S + I + R) - \mu S - \lambda \beta SI$$

$$(2 \text{ brucel model}) \quad (dI/dt) = \lambda \beta SI - \mu I - \gamma I$$

$$(3 \text{ brucel model}) \quad (dR/dt) = pS - \mu R$$

$$(4 \text{ brucel model}) \quad R_0 = \lambda \beta S / (\gamma + \mu)$$

The parameter for p_c *critical immunisation level for eradication* remains unmodified as above:

$$(5 \text{ brucel model}) \quad p_c = 1 - (1/R_0)$$

Thus, to set the target levels of immunisation for elimination (defined as *critical immunisation level for eradication* (p_c)) estimates of the *effective reproduction ratio* (R_e) were needed based on the epidemiological and demographic data. We needed

therefore, derived from the equations (1 brucel model) to (5 brucel model), results for the following seven parameters:

- μ (mortality rate)
- α (birth rate)
- β (transmission coefficient)
- γ (recovery rate)
- η (prevalence-dependent reduction of birth rate), and
- λ (proportion of infectious)
- ve (vaccine efficacy)

The equations for fitting demography and parasite biology, and for defining the critical immunisation level for eradication, are summarised as follows:

Nr.	Equation	Content
(1)	$dU/dt = \mu(U+W+V) - \mu U - \beta UW$	susceptibles
(2)	$dV/dt = \beta UW - \mu V - \gamma V$	infectious group
(3)	$dW/dt = \gamma V - \mu W$	immune group
(4)	$Ro = \beta U / (\gamma + \mu)$	Basic reproduction ratio
(5)	$p_c = 1 - (1/Ro)$	Critical immunisation level for eradication.

As these equations have no unique solution, estimates were obtained by a mathematical modelling process. *Table 6.1.* gives an overview on the parameters used to fit the brucellosis transmission.

Table 6.1.: List of fitted parameters to transmission in small ruminants

Parameter		Simulation	
Symbol	Description	Initial value	reference
S	The susceptible population (= all sheep & goats minus the sero-positive and minus the vaccinated animals)	From database	Data collected for this thesis ⁵⁵
I	The infected populations (= the number of sero-positive sheep & goats calculated out of the prevalence, which has been calculated out of the sampling)	From database	
R	The immune population (=the vaccinated sheep & goats)	From database	
ve	Vaccination efficacy	0.65	(Zinsstag J. et al, 2005a)
α	Per capita annual birth rate	0.8	(Zinsstag J. et al, 2005a)
μ	Per capita annual death rate	0.8	(Zinsstag J. et al, 2005a)
β	Transmission coefficient	$1.56e^{-1}$	(Zinsstag J. et al, 2005a)
γ	Per capita annual recovery rate of infected animals	0	(Zinsstag J. et al, 2005a)
λ	Proportion of infectious sero-positive animals	RANDOM UNIFORM (0.2, 0.8)	(Zinsstag J. et al, 2005a)
η	Prevalence-dependent reduction of birth rate	RANDOM UNIFORM (0.15 , 0.5)	(Zinsstag J. et al, 2005a)

In a first step, α and μ (*birth_(baseline)* and *mortality rate*) have been optimised for N, representing *all animals*, the *Susceptible*, *Infectious* and *Immune*. In other words, the

⁵⁵ (Food and Agriculture Organisation of the United Nations, Rome, 1977) (Kolar J., 2003) (Ministry of Agriculture and Food, 1998) (Ministry of Agriculture, 2003b) (Ministry of Agriculture, 2003a) (State Statistical Office of Mongolia, 1996) (Ministry of Agriculture, 2003c) (State Statistical Office of Mongolia, 1974) (State Statistical Office of Mongolia, 1999) (National Statistical Office of Mongolia, 2003) (State Veterinary & Animal Breeding Department of the Ministry for Food & Agriculture, 2003) (State Veterinary & Animal Breeding Department of the Ministry for Food & Agriculture, 2002; State Veterinary & Animal Breeding Department of the Ministry for Food & Agriculture, 2001) (State Veterinary & Animal Breeding Department of the Ministry for Food & Agriculture, 1999) (State Veterinary & Animal Breeding Department of the Ministry for Food & Agriculture, 1998) (Agriculture Organisation, Ministry of Agriculture et al, 1997) (State Veterinarian Administration Office, 1996) (State Veterinarian Administration Office, 1994) (State Veterinarian Administration Office, 1993) (State Veterinarian Office, 1991) (State Veterinarian Office, 1990a) (State Veterinarian Office, 1990b) (State Veterinarian Office, 1989) (State Veterinarian Office, 1988) (State Veterinarian Office, 1987) (State Veterinarian Office, 1985) (State Veterinarian Office, 1984) (State Veterinarian Office, 1983) (State Veterinarian Office, 1982) (State Veterinarian Office, 1981) (State Veterinarian general Office of the Ministry of Agriculture, 1980) (State Veterinarian Office, 1979) (State Veterinarian Office, 1978) (State Veterinarian Office, 1977)

baseline birth rates were expressed proportionally to the total populations. The mortality parameters in livestock included natural mortality and off take. In a second step β (*transmission coefficient*) were fitted by fixing the demographic parameters that resulted from the demographic fit. As shown above γ (*recovery rate or immunity loss parameter*) was set at zero: a seropositive animal remains seropositive for the rest of its life (Nicoletti P. in (Madkour M., 2001)). The parameter η (*prevalence-dependent reduction of birth rate*) was expressed as uniform probability distribution (0.15, 0.5) (Zinsstag J. et al, 2005a). The parameter λ (*proportion of infectious*) was set at 0.8, which is the upper limit of the estimate of the previous work (Zinsstag J. et al, 2005a). That leads to a more conservative estimate of the *critical immunisation level for eradication*. For the fitting of the deterministic equations to the data we applied Vensim™ system-analysis software⁵⁶ using the Powell nonlinear maximum-likelihood optimisation algorithm (Zinsstag J. et al, 2005a). The parameters were fitted on the basis of the goodness-of-fit⁵⁷ comparing the log likelihood of the current model with the log likelihood of a perfect model (Zinsstag J. et al, 2005a).

Fitting the model to the data

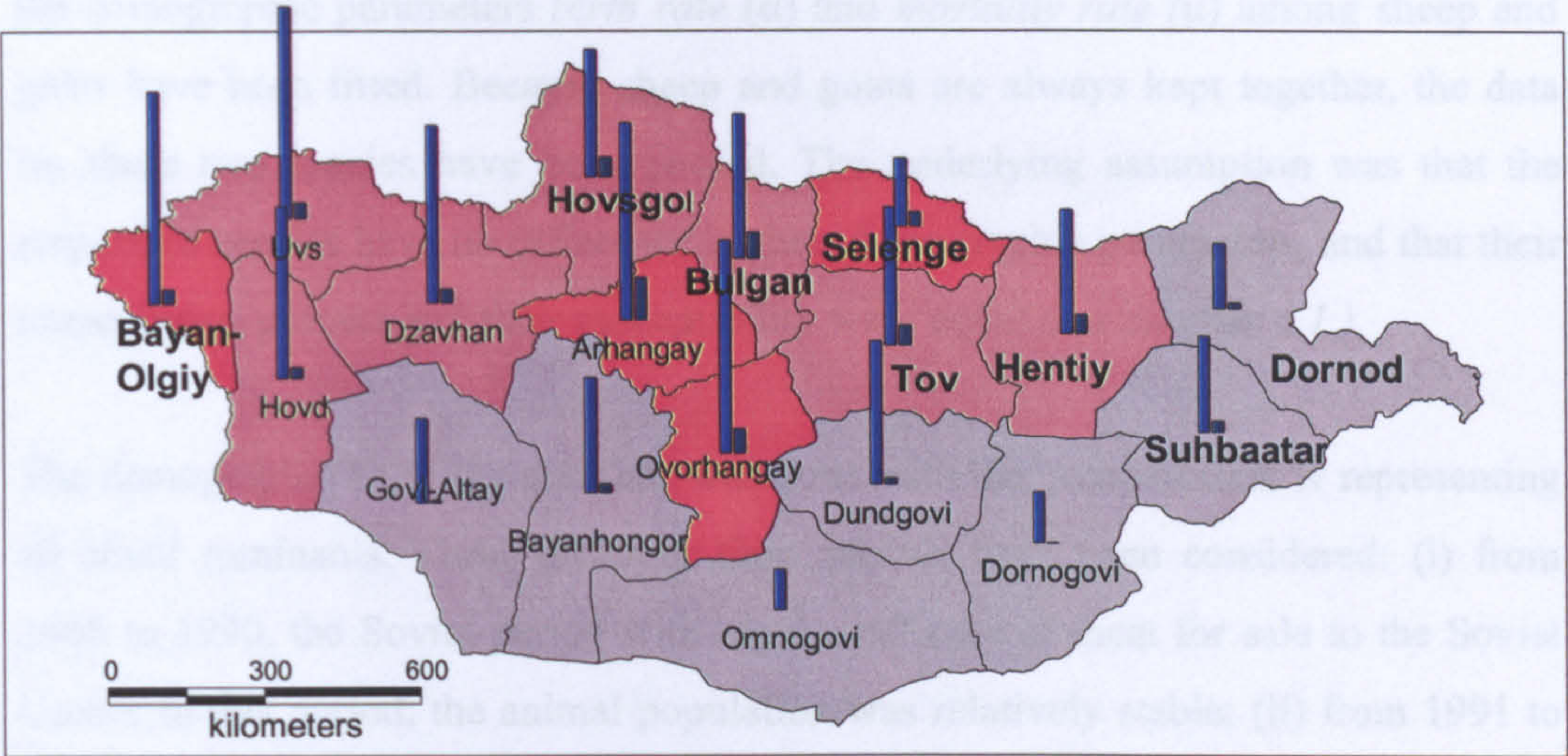
The mathematical analysis on the vaccination has been done for 8 Aimags⁵⁸, selected because they were the first 8 Aimags participating in the whole herd vaccination programme in SR, which took place during 1975 to 1985 (*see chapter 5*). The initial vaccination in these Aimags has been undertaken with the assistance of WHO experts in the year 1975 to 1977. These Aimags are located in East, North-East, North and West of Mongolia. Both human and animal population density are higher than in the southern part of Mongolia with the Gobi desert and lower than in the central part of Mongolia (*figure 6.4.*). The selected Aimags belonged at that time to the most endemic areas of the country (*figure 6.5.*).

⁵⁶ Ventana Systems Inc., 60 Jacob Gates Road, Harvard, MA, USA; www.vensim.com

⁵⁷ In Vensim™ “goodness-of-fit” is called “payoff” which is the same as the deviance in maximum likelihood estimation. The best model is the one with the smallest payoff.

⁵⁸ Selenge, Bulgan, Bayan-Olgii, Dornod, Suhbaatar, Hovsgol, Hentiy and Tov.

Figure 6.4.: Population densities in humans and animals, 1970



Derived from material collected for this thesis

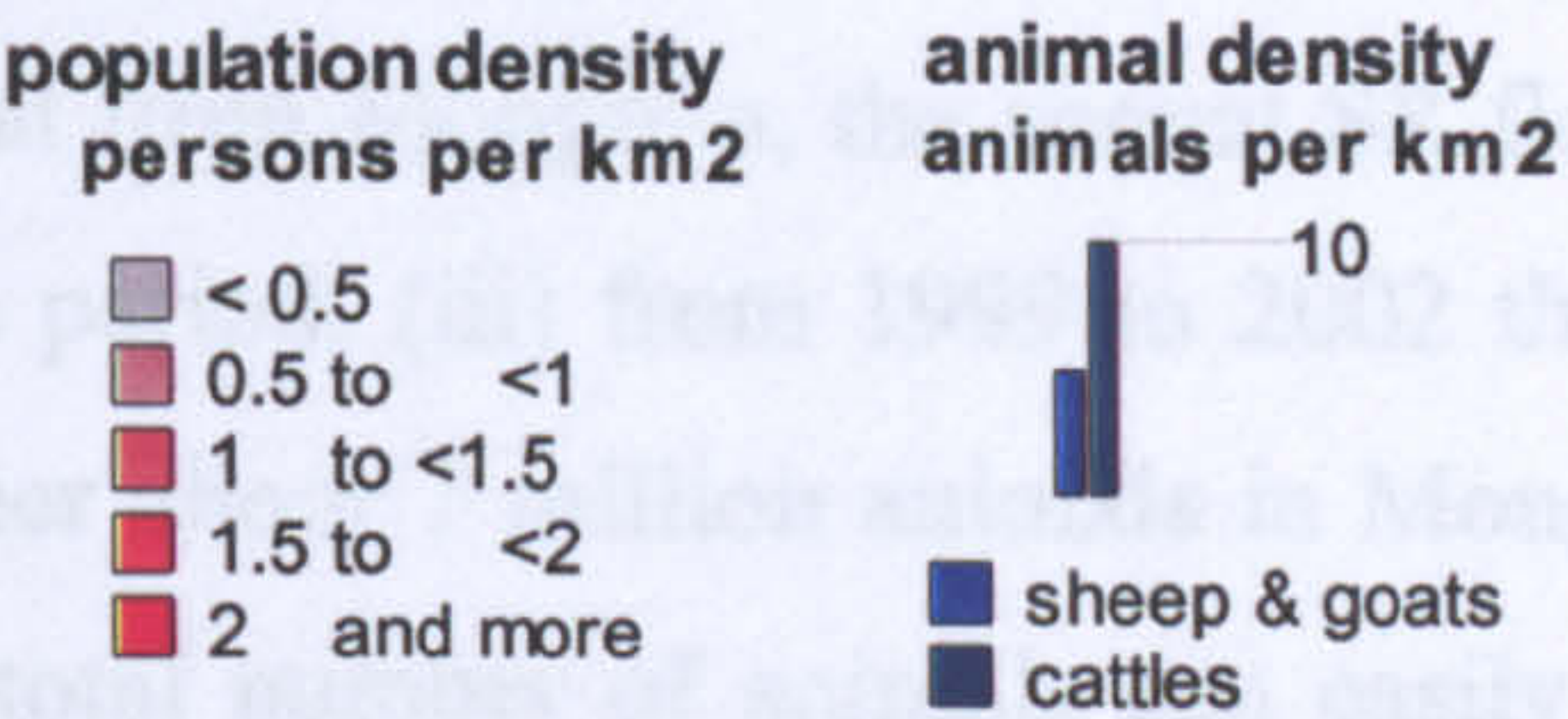
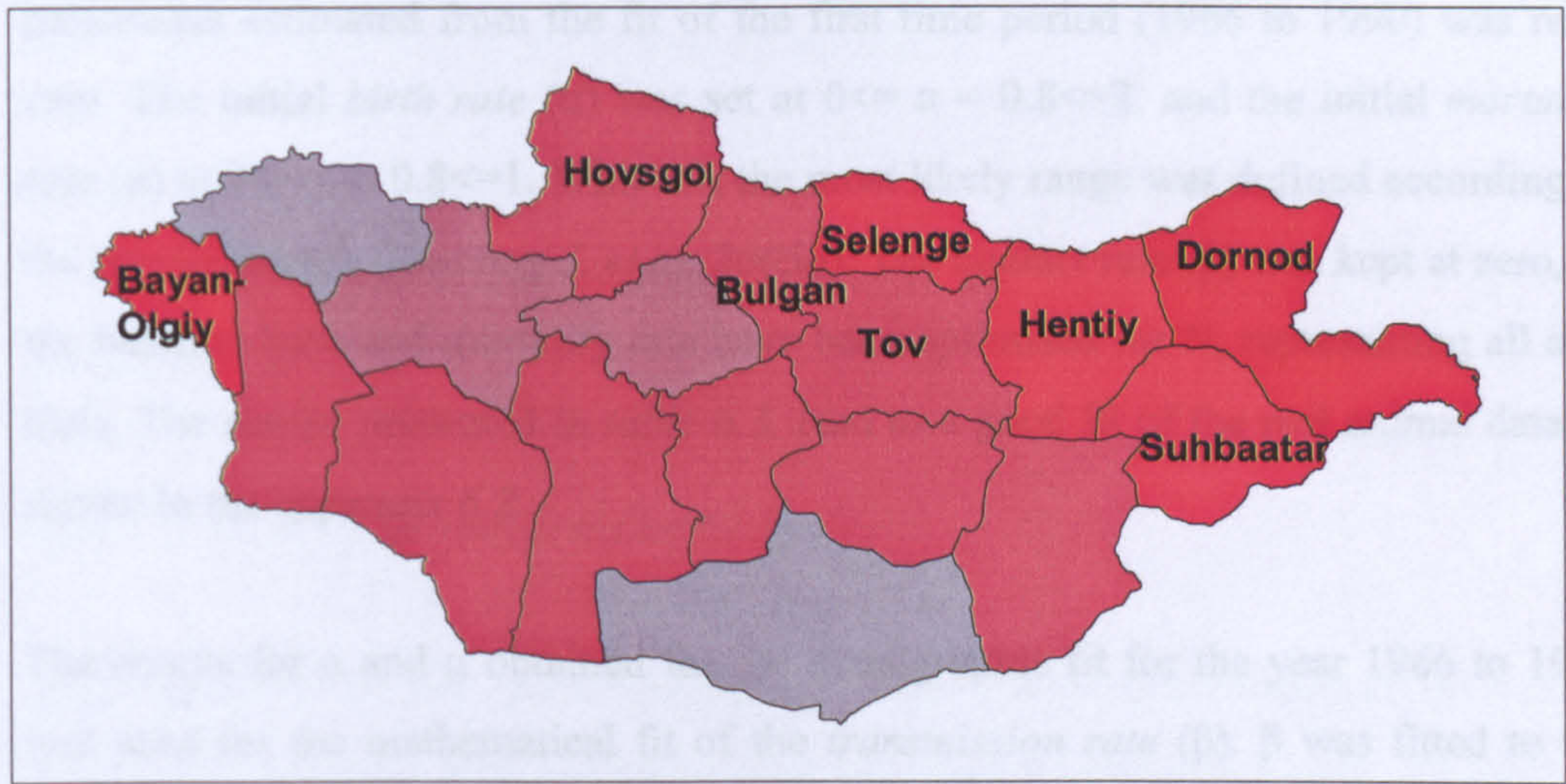
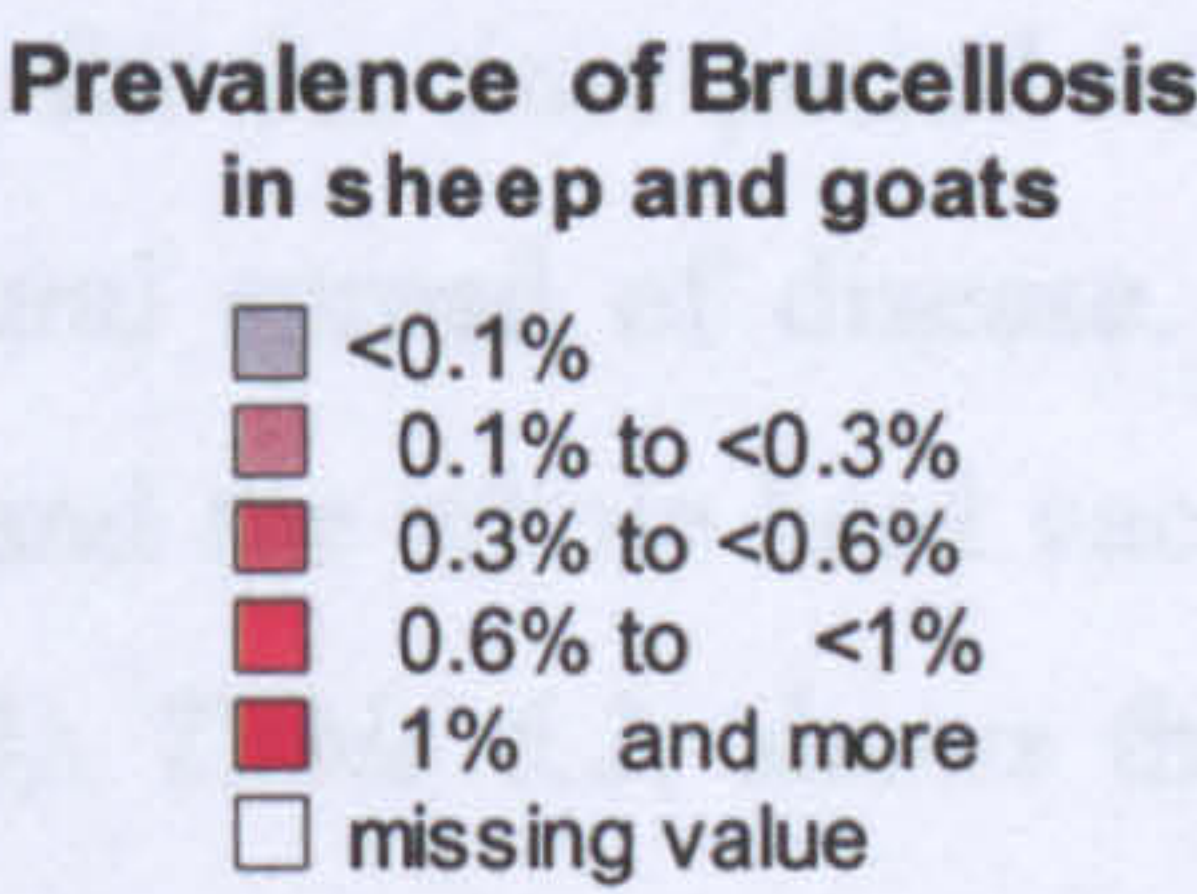


Figure 6.5.: Brucellosis prevalence in small ruminants in 1975



Derived from material collected for this thesis



In a first step of the mathematical analysis, the brucellosis *transmission rate* (β) and the demographic parameters *birth rate* (α) and *mortality rate* (μ) among sheep and goats have been fitted. Because sheep and goats are always kept together, the data for these two species have been pooled. The underlying assumption was that the respective species have no difference in their demographic parameters, and that their transmission process and their susceptibility were equal (*see chapter 4.1.*).

The demographic fit to the real data was done with the compartment N representing all small ruminants. Three different time periods have been considered: (i) from 1966 to 1990, the Soviet period with regular off take of meat for sale to the Soviet Union. In this period, the animal population was relatively stable; (ii) from 1991 to 1999, the post Soviet period, where livestock production has been privatised and the Soviet Union could not any longer import meat from Mongolia, the annual SR flock rose by approximately 4% annually over this period; (iii) from 1999 to 2002 three consecutive Dzud catastrophes killed altogether about 7 million animals in Mongolia, the effect these time periods had on the total number of animals can easily be seen in the *appendix 6.2.*. For the further mathematical modelling, the demographic parameters estimated from the fit of the first time period (1966 to 1990) was relevant. The initial *birth rate* (α) was set at $0 \leq \alpha = 0.8 \leq 2$, and the initial *mortality rate* (μ) at $0 \leq \mu = 0.8 \leq 1$. With this the most likely range was defined according to the previous work (*Zinsstag J. et al, 2005a*). The contact rate (β) was kept at zero, as the baseline birth and mortality rate have been optimised for N, representing all animals. The results presented in *table 6.3.* lead to a good fit of the real animal data as shown in the *appendix 6.2.*.

The results for α and μ obtained for the demographic fit for the year 1966 to 1990 was used for the mathematical fit of the *transmission rate* (β). β was fitted to the data of the *susceptible* (S) and *infected* (I) SR for the time period with no disease control interventions, to best observe the natural spread of disease. The *test and slaughter* campaigns came to an end in 1968, and the whole herd vaccination campaign started gradually in 1975 (*see chapter 5*). *Table 6.2.* shows the time period

with no intervention which could be used for fitting the *transmission rate* (β) in the different Aimags.

Table 6.2.: Time period used to fit transmission rate

Aimag	T&S up to:	Start vaccination campaign	Observation period used to fit β (t1 - t2)
Bulgan	1968	1975	1969 - 1974
Selenge	1968	1975	1969 - 1974
Bayan-Olgii	1968	1976	1969 - 1975
Dornod	1968	1976	1969 - 1975
Suhbaatar	1968	1976	1969 - 1975
Hovsgol	1968	1977	1969 - 1976
Hentiy	1968	1977	1969 - 1976
Tov	1968	1977	1969 - 1976

β = *transmission rate between animals*

The initial data for the compartments of the *susceptible* (S) and *infectious* (I) animals were derived with help of the following equations:

$$(6) \; S_t = N_t - I_t - R_{tcum}$$

$$(7) \; I_t = prev_t * N_t$$

$$(8) \; R_{tcum} = R_t (1 + (1-\mu) + (1-\mu)^2 + (1-\mu)^3)$$

This underlines the *loss of vaccination immunity*. The vaccinated animals are becoming susceptible again four years after their vaccination (Zinsstag J. et al, 2005a).

$$(9) \; prev_t = (seropositive\;sheep_t + seropositive\;goats_t) / (sample\;sheep_t + sample\;goats_t)$$

This equation (9) has been applied under the condition that the data were available for the seropositive and sample size for both sheep and goats. Otherwise, the following equation has been applied:

$$(9_{\text{alternative 1}}) \text{prev}_t = ((\text{seropositive sheep}_t) / (\text{sample sheep}_t))$$

or

$$(9_{\text{alternative 2}}) \text{prev}_t = ((\text{seropositive goats}_t) / (\text{sample goats}_t))$$

The data collection contributed to feed the following compartments:

N_t = all sheep and goats

R_t = all vaccinated sheep and goats

seropositive sheep;

seropositive goats;

sample size of sheep;

sample size of goats.

In the modelling process the payoff variables S and I were weighted by

$$1/\text{Std}(\Sigma S_{t1 \text{ to } t2})$$

against

$$1/\text{Std}(\Sigma I_{t1 \text{ to } t2})^{59}$$

according to the manual of the Vensim Software⁶⁰.

The most likely range was defined with

$$0 \leq \text{animal contact rate} = 1.56e^{-7} \leq 0.1$$

⁵⁹ t1 is the first year of observation (1969), t2 is the last year of observation see *table 6.2*.

⁶⁰ In the fitting process the different compartments have different sizes with 100 or 1000 fold differences. To account for these differences in the fitting process parameter estimates are done by accounting for a weighting between compartments at different size. The weighting is done by dividing compartment size by 1/Std..

considering the previous work (Zinsstag J. *et al*, 2005a). The summary of the results is presented in *table 6.3.* The *appendix 6.3.* illustrates this fit of β for all eight Aimags.

Assessing the vaccination coverage

In a second step of the mathematical analysis, the target levels of vaccination for elimination of brucellosis in the various Aimags (p_c) were calculated in Microsoft Excel. For this, the *effective reproductive ratio* (Re) was calculated for every year during the observation time period as shown in the *table 6.2.* The equations applied were as defined above:

$$(4_{\text{new}}) Re_t = \lambda \beta S_t / (\gamma + \mu)$$

$$(5_{\text{new}}) p_{ct} = 1 - (1/Re_t)$$

$$(6) S_t = N_t - I_t - R_{tcum}$$

The parameters λ (*proportion of infectious seropositive animals*) and γ (*recovery rate of infected animals*) were set as shown in *table 6.1.* and described above on page 149 ($\lambda = 0.8$; $\gamma = 0$). The parameters *transmission rate* (β) and *mortality rate* (μ) resulted from the mathematical fitting process with Vensim™ system-analysis software.

Table 6.3.: Results on demographic and transmission parameters, and on critical immunisation level for eradication

Aimag	Demographic parameters			Transmission parameter		pc	
	obs. year	α	μ	obs. year	β	average	CI 95%
Selenge	1966 - 90	0.80	0.79	1969-74	7.36E-06	53.74%	0.16%
Bulgan	1966 - 90	0.80	0.80	1969-74	2.76E-06	48.00%	0.10%
Bayan-Olgii	1966 - 90	0.81	0.80	1969-75	1.74E-06	38.15%	0.08%
Dornod	1966 - 90	0.80	0.80	1969-75	2.51E-06	49.42%	0.05%
Suhbaatar	1966 - 90	0.79	0.80	1969-75	2.01E-06	35.28%	0.12%
Hentiy	1966 - 90	0.81	0.80	1969-75	1.73E-06	40.55%	0.05%
Hovsgol	1966 - 90	0.80	0.80	1969-76	1.38E-06	39.60%	0.82%
Tov	1966 - 90	0.81	0.80	1969-76	1.58E-06	37.70%	0.11%

α birthrate

μ mortality rate

β transmission rate between animals

pc critical immunisation level for eradication

Finally, in a third step of the mathematical analysis, the effective vaccination policy for the time period 1975 to 1985 (and later up to 2002) was compared with the target level of vaccination for elimination (p_c). Thus, the difference between the *proportion of protected* (pp) and the *threshold vaccination coverage* (p_c) was calculated in Microsoft Excel. The *proportion of protected* (pp) was calculated out of the *vaccine coverage* (R_{cum}), as in equation (8), and corrected by the *vaccine efficacy*. The *vaccine efficacy* indicates the power or capacity of the vaccine to protect from infection. The vaccine efficacy was set at 65%, as in the prior studies (Zinsstag J. et al, 2005a). With this the vaccine specificities of Rev.1, and the local conditions such as losses due to cold-chain deficiency were considered. As benchmark for assessing the vaccination policy, new calculated *threshold vaccination coverage* ($p_{c\ t1\ to\ t2}$) was used, taken from the average of the observation period as shown in table 6.2..

$$(10) \ p_{c\ t1\ to\ t2} = (\sum p_{c\ t1\ to\ t2}) / n$$

n = number of observation years, so between 6 and 8 observation years (1969 to 1974, or 75, or 76).

This benchmark defined the fraction of the animal population which needed to be vaccinated to eliminate brucellosis. Thus, to assess the yearly vaccination policy, the effective yearly proportion of protected (pp_t) was compared with the target level of vaccination for elimination (p_{ct1-t2}).

(11) Discrepancy of vaccination level from required vaccination level_t = $pp_t - p_{ct1-t2}$

The results of the equation (11) are given in *table 6.4.* and as a graph in *figure 6.6.*. This finally gave the hint on the appropriateness of the chosen vaccination policy, compared to the effective local demographic and epidemiological situation. The graphical view with the development of the brucellosis prevalence, the vaccination policy, and the corresponding result about the policy assessment is given in the *appendix 6.4.*.

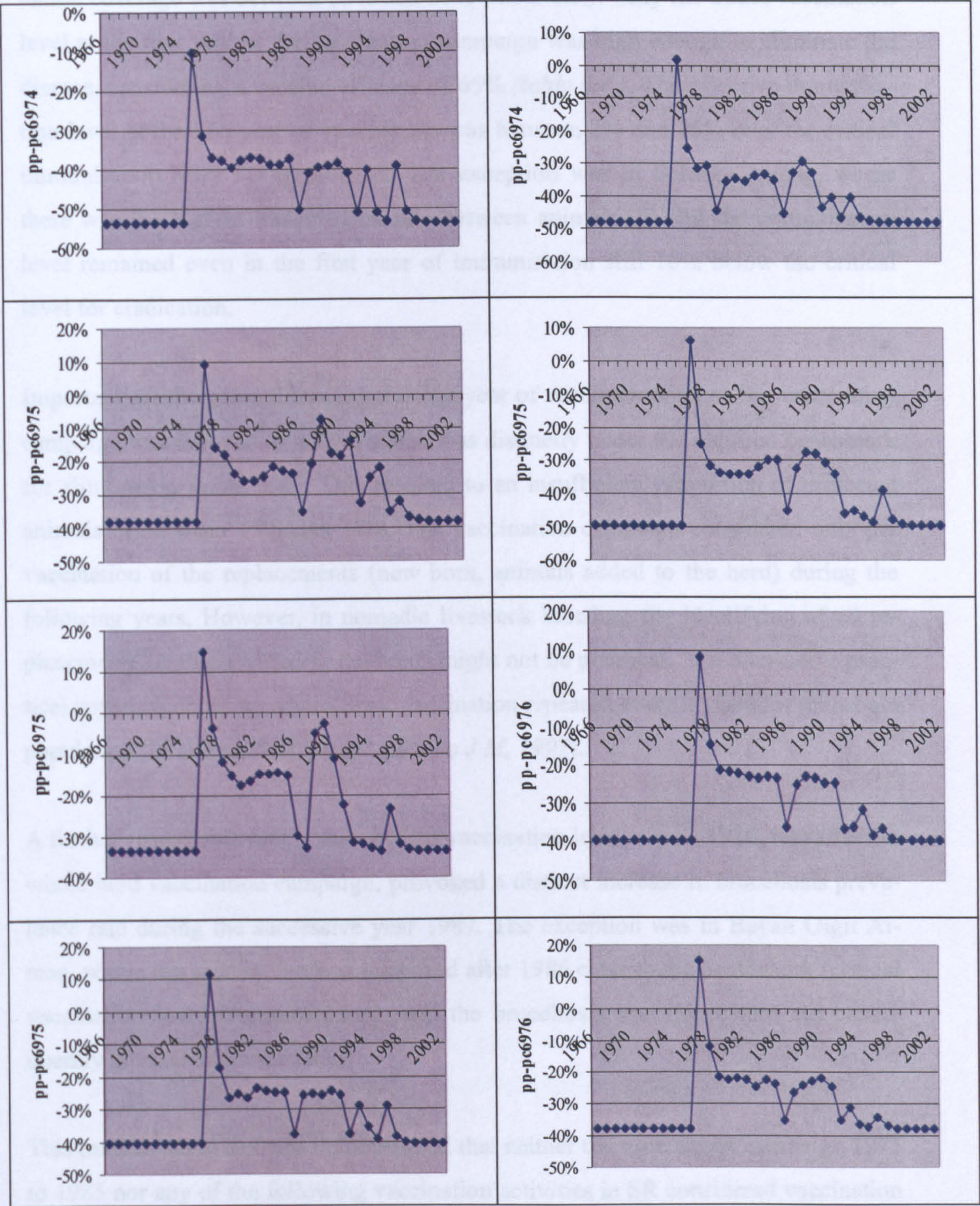
Table 6.4.: Discrepancy from actual to required immunisation level

Aimag	pc (t1 - t2) average	pp		pp - pc(t1 - t2)	
		v1	v2 - 1985	v1	v2 - 1985
Selenge	53.74%	43%	16%	-10%	-37%
Bulgan	48.00%	50%	14%	2%	-34%
Bayan-Olgii	38.15%	47%	16%	9%	-22%
Dornod	49.42%	55%	18%	6%	-32%
Suhbaatar	35.28%	48%	20%	13%	-15%
Hentiy	40.55%	52%	16%	11%	-24%
Hovsgol	39.60%	48%	18%	8%	-21%
Tov	37.70%	53%	16%	15%	-21%

pc (t1 - t2) critical immunisation level for eradication in observation period
 pp proportion protected = vacc. cov. * vacc. efficacy (here 65%)
 pp-pc(t1 - t2) discrepancy of immunisation level from required immunisation level
 v1 first year of vaccination
 v2 - 1985 average for second year of vaccination up to end of vacc. campaign (1985)

Figure 6.6.: Discrepancy from actual to required immunisation level

(graph to table 6.4.) (from left to right: Selenge, Bulgan, Bayan Olgii, Dornod, Sukhbaatar, Khuvsgol, Khentii and Tuv)



Derived from material collected for this thesis

Discussion on the results

The results among the Aimags are close together and consistent, the threshold vaccination coverage was between 35% and 53% (*table 6.3.*). Only the initial vaccination level at the first year of the vaccination campaign was high enough to eliminate the disease, considering a vaccine efficacy of 65% (*table 6.4.*). The effective immunisation level in the first year of vaccination was between 2% and 15% over the critical immunisation level for eradication. The exception was in Selenge Aimag, where there was the highest transmission rate between animals (β) and the immunisation level remained even in the first year of immunisation still 10% below the critical level for eradication.

Important are the years following the first year of vaccination, when the vaccination campaign was dropped to a level which was distinctly under the required benchmark for elimination (*table 6.4.*). This resulted to an insufficient proportion of protected animals of between 15% and 37%. The vaccination campaign considered only the vaccination of the replacements (new born, animals added to the herd) during the following years. However, in nomadic livestock breeding the identifying of all replacements (animals added to the herd) might not be practical. "An alternative practical approach could be whole-flock vaccination repeated every 2 years for the whole population for at least 8-10 years" (*Blasco J M, 1997*).

A further remarkable fact is that the low vaccination level in year 1986, just after the whole herd vaccination campaign, provoked a distinct increase in brucellosis prevalence rate during the successive year 1987. The exception was in Bayan Olgii Aimag, where the vaccination was increased after 1986 close to the benchmark (critical vaccination level for eradication), and the brucellosis prevalence rate did consequently not increase after 1986.

This mathematical analysis demonstrated that neither the vaccination campaign 1975 to 1985 nor any of the following vaccination activities in SR considered vaccination coverage sufficient to eradicate brucellosis. To fight brucellosis successfully vacci-

nation level like that of the first year of the vaccination campaign in SR (1975 to 85) would have been required, but this was not kept up in the following years. On the assumptions as described in *table 6.1.*, and vaccine efficacy 65%.

Statistical analysis on the animal human transmission

The qualitative analysis of the surveillance policy in the first part of this chapter has shown that the first vaccination campaign, starting in the 1970s, focused on the immunisation of SR. This seemed to be justified, as most etiological analysis concluded *B. melitensis* as the major source of brucellosis infection in humans. The SR had been identified as the relevant animals for the spread of infection in humans. Occupational activities have been recognised as by far the most important route of transmission. In the 1980s, the focus of surveillance had shifted to cattle in dairy farms. With this policy change the prevention had then to be set to prevent food borne infection, so to assure that cow's milk was not contaminated with *Brucella*. In none of the policy papers or publications, could evidence for this policy shift be found. Because Russian experts were considerably involved in developing this new policy, the original motivation may have been based on external trade opportunities, and the sale of milk and meat products to the USSR.

Multiple Regression Analysis

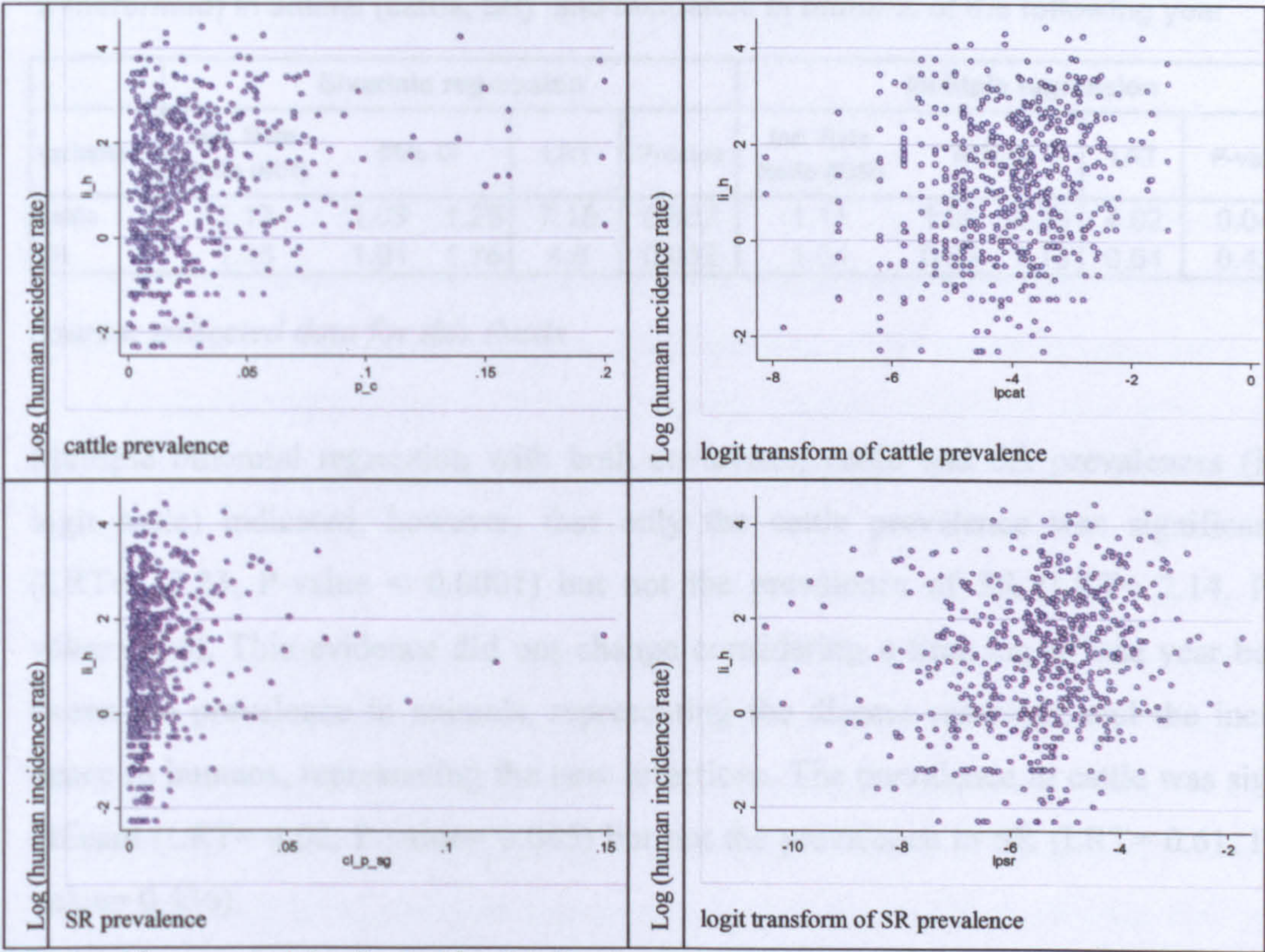
This thesis has provided empirical evidence on the spread of brucellosis in animal and humans and opened up the possibility to test, using statistical regression analysis, the dependency of the infection in humans upon the infection in the different kinds of animal. It was expected with this analysis to get a clearer view about which kind of animal the disease in humans came from and to therefore know where to put the focus for disease control.

Bivariate negative binomial regression analyses have been applied to assess the relation between human incidence (outcome) and animal prevalence (cattle, SR). Let x_i

be the number of human brucellosis cases for year i , and N_i be the human population size during year i . We assume that x_i has a negative binomial distribution, that is $x_i \sim \text{NB}(p_i, r)$, where r is the extra-Poisson variation, and p_i is related to the mean parameter μ_i via the equation $p_i = (r / (r + \mu_i))$. We model the relationship between human incidence and animal prevalence by the equation $\log(\mu_i) = a + \beta Z_i + \log(N_i)$, where Z_i is the annual prevalence in animals, a is the constant, and β quantifies the magnitude of the association between human incidence and animal prevalence.

The logit transformation was applied to the animal prevalence to make the relationship with human incidence more linear (*figure 6.7.*).

Figure 6.7.: Correlation between human incidence and animal prevalence



Derived from material collected for this thesis

Significance was assessed at 5% significance level using the likelihood ratio test (LRT). The results (*table 6.5.*) show a significant positive association between hu-

man incidence and prevalence in cattle (incidence rate ratio IRR 1.24, 95% CI 1.14, 1.35) as well as prevalence in SR (incidence rate ratio IRR 1.16, 95% CI 1.08, 1.24).

Table 6.5.: Results on animal – human transmission

Negative binomial regression to assess the relation between the prevalence (logit transformed) in animal (cattle, SR) and incidence in humans

	Bivariate regression					Multiple regression				
variable	Inc. Rate Ratio (IRR)	95% CI		LRT	P-value	Inc. Rate Ratio (IRR)	95% CI		LRT	P-value
cattle	1.24	1.14	1.35	22.44	<0.0001	1.21	1.09	1.34	12.23	<0.0001
SR	1.16	1.08	1.24	15.32	<0.0001	1.07	0.98	1.17	2.14	0.140

Negative binomial regression to assess the relation between the prevalence (logit transformed) in animal (cattle, SR) and incidence in humans of the following year

	Bivariate regression					Multiple regression				
variable	Inc. Rate Ratio (IRR)	95% CI		LRT	P-value	Inc. Rate Ratio (IRR)	95% CI		LRT	P-value
cattle	1.13	1.03	1.23	7.18	0.007	1.11	1.00	1.23	4.02	0.045
SR	1.08	1.01	1.16	4.6	0.032	1.04	0.95	1.13	0.61	0.436

Source: collected data for this thesis

Multiple binomial regression with both covariates, cattle and SR prevalences (in logit scale) indicated, however, that only the cattle prevalence was significant (LRT= 12.23, P-value < 0.0001) but not the prevalence of SR (LRT= 2.14, P-value=0.14). This evidence did not change considering a time lag of one year between the prevalence in animals, representing the disease reservoir, and the incidence in humans, representing the new infections. The prevalence in cattle was significant (LRT= 4.02, P-value= 0.045) but not the prevalence in SR (LRT= 0.61, P-value= 0.436).

This is strong evidence, as both multiple regression analyses showed only cattle prevalence being significant for the infection in humans.

Discussion on the results

The etiological analysis had concluded that, in the Mongolian context, SR rather than cattle were the source of infection in humans (*see chapter 4*). This was based on observations and analysis carried out in the late 1960s and early 1970s, as well as research in the 1980s, which all had come to the conclusion, that the incidence of brucellosis in human was more closely linked to the disease reservoir (prevalence) in SR than in cattle (*see chapter 4*).

Relying on this, the control policy from the mid 1970s onwards had been based for 10 years on the whole herd vaccination of SR. Only in the late 1980s, was the focus changed and put more on the control in cattle, mainly in dairy farms. However, scientific evidence for this policy shift was not found in the Mongolian papers. It could therefore be assumed that the motivation was related to assure trade opportunities with Russia.

The data allowed a multiple regression analysis to be applied. This suggested that the data quality was good, as a clear and consistent pattern was indicated in the results. The results showed that only the prevalence in cattle but not the prevalence in SR was significantly linked to the incidence in humans. This may have given evidence for explaining the policy shift as described above. But still, an inconsistency remained.

A contradiction appeared between the traced Mongolian scientific literature, and the data collected in Mongolia. The scientific literature concluded that the SR and *B. melitensis* were the main source of infection in humans, and that the contact with animals rather than alimentation was the route of transmission. The data on the other side proved that cattle were the source of infection, so mostly *B. abortus*, and that the route of transmission was most likely food borne.

In fact both results are plausible, as the source of human brucellosis infection can be both, SR or cattle, and the route of transmission can be food borne or related to oc-

cupational activities (*see chapter 2*). Looking at the different possibilities leading to this apparent inconsistency provided better understanding.

The etiological analysis was based on surveys among high-risk population groups. So the surveys focused mainly on herders, workers in slaughterhouses or processing animal products such as hides or wool, and on veterinarians. These surveys provided the evidence for the main source of disease being in SR more than cattle, and the main route of transmission being contact rate over food borne pathways. Studies among herders from the 1970s up to the 1990s described an infection rate in herders of about 30% over decades (*see chapter 4*).

On the other side, the data used in the multiple regression analysis of this work has been generated in a different way: the rates on human incidence, applied in this analysis, had been calculated from laboratory confirmed cases reported from the Aimag centres to the central authorities in Ulaanbaatar. Only brucellosis cases confirmed by serological laboratory were included in the reporting (personal communication with Dr. Altantsetseg, deputy director of Public Health Organisation of Khuvsgul Aimag (*Roth F., 2003a*)). And the present analysis of this data leads to the identification of cattle as the source of infection. Thus, we conclude, given this “contradictory” finding that the most vulnerable and concerned group, the herders, were not represented in the reported data used in this thesis’s analysis.

This has important policy implication, for only confirmed cases by serological laboratory would have had access to appropriate treatment with drugs (personal communication with Dr. Tserendolger, director of Soum Hospital in Khutgul (*Roth F., 2003a*)). The data analysis showed that the cases represented in the reported data, were patients infected through cattle. It can be assumed that they had most likely been infected by the consumption of milk, and that they were most likely living in urban areas buying the milk in uncontrolled markets. Being registered in the files meant they had been diagnosed with laboratory serology and had access to treatment. We have seen that the access to diagnosis and health care was very limited, as nearly half of the brucellosis patients already suffered from the chronic form of dis-

ease (see chapter 4). The multiple regression analysis has suggested that the main risk groups, the herders, were not included in the data. Therefore, the access to brucellosis diagnosis and appropriate treatment was likely limited or non-existent for these groups. This is in line with observations made during the field work in the Soum Hospital in Khutgul, and in the Aimag Hospital in Moron, both in Khuvsgol Aimag.

Human brucellosis was a considerable problem in this area. To access treatment, the patients had first to come to the Soum hospital, Khutgul Hospital, for clinical diagnosis and referral to the Aimag Centre Hospital in Moron for serological laboratory tests (personal communication with Dr. Tserendolger, director of Soum Hospital in Khutgul (Roth F., 2003a)). This meant several days of horse riding, or very expensive car drives - unrealistic for most patients. The waiting lists to get treatment were long, as only five beds were allocated to patients ill from brucellosis in Moron hospital (personal communication with Dr. Narantsetseg, general epidemiologist in Central Aimag Hospital, Moron (Roth F., 2003a)). But before getting treatment, serological laboratory diagnosis was needed. Because of lack of funds and proper diagnostic tools, the Aimag Centre Hospital in Moron could only diagnose *B. abortus* (personal communication with the bacteriologist, Central Aimag Hospital, Moron, and with Dr. Narantsetseg, general epidemiologist in Central Aimag Hospital, Moron (Roth F., 2003a)). If the patient succeeded in getting to Khutgul for clinical diagnosis, and then to Moron for laboratory diagnosis, and if the patient had the "luck" to suffer from *B. abortus*, and not from *B. melitensis* (more likely as the patient was a herder), and was properly diagnosed, then she or he would have needed further luck to get one of the five beds available. The treatment could then start which could last for 45 days, but patients were treated only for 10 days in the hospital, and had to finance the drugs for the remaining 35 days themselves. Thus, most patients stopped treatment after 10 days because of lack of money (personal communication with Dr. Tserendolger, director of Soum Hospital in Khutgul, and confirmation by Dr. Narantsetseg, general epidemiologist in Central Aimag Hospital, Moron (Roth F., 2003a)). These documented observations show at what point the access to treatment against brucellosis was limited for herders.

It is important, when interpreting the data, to consider that the limited access to treatment (and with this the reported data) may also have existed under the socialist regime. Thus, the “data collection” may be consistent over the different regimes. This was illustrated with the following testimony (personal communication with Dr. Altantsetseg, deputy director of Public Health Organisation of Khuvsgul Aimag (*Roth F., 2003a*)): In 1988/89 Dr. Altantsetseg was working as physician in a Soum hospital. Physicians coming from Ulaanbaatar had conducted a serological survey on human brucellosis; among others, all herders of her Soum were included, however, they never reported the result of the survey to her hospital. As consequence, none of the sero positive brucellosis patients could be identified and treated. Even when the identities of the sero positive cases were known, they could not be treated, as the official confirmation, from the authorities conducting the surveys, were not available. This happened to four member staff of the Soum hospital.

Summary of Finding

The quantitative analysis has pointed out two potential weaknesses of the surveillance policy:

- (i) the vaccination coverage did not reach the critical vaccination level for eradication;
- (ii) the applied case definition for humans (laboratory confirmation) did not consider the limited access to laboratories. The consequences were untreated patients and under-reporting.

The findings of the qualitative and quantitative analysis are further discussed in the next *chapter 7* to make recommendations for surveillance policy (*aim 4, see chapter 3*).

Discussion and recommendations

1. Overview

The aim of this thesis was to estimate the effectiveness of the brucellosis surveillance policies applied in Mongolia to provide recommendations for future surveillance policies. Historically, Mongolia has had a long tradition of efforts to control this disease, but until now little was known about its degree of success. The intent of this work, therefore, was to address this critical gap and create an evidence base to formulate policy recommendations.

To achieve its major aims, this thesis had four investigative steps: The first step (Aim 1) was to compile the evidence of the epidemiological patterns of brucellosis. The second step (Aim 2) was to establish an historical overview of the different strategies applied to control brucellosis. Aimag based information, from 1966 to 2002 onwards, was therefore obtained, using intensive archive searches and interviewing of key persons, to assemble a comprehensive database on the spread of brucellosis in cattle, sheep, goats, and humans, and the brucellosis control policies. The etiology of brucellosis in Mongolia was elaborated from Mongolian scientific works and reports from international technical experts. Together, the knowledge on the specific etiology and the empirical evidence, provide a comprehensive picture of the epidemiology of brucellosis in Mongolia (*see chapter 4*). Policy papers, reports, as well as testing and vaccination data accumulated over the years by the author have provided a comprehensive and historical review of the Mongolian surveillance policies (*see chapter 5*). The data collections on the epidemiology of brucellosis and the surveillance policies have been mainly carried out in Mongolia, and were assisted by a Mongolian researcher partner⁶¹ to assure access to the archives, facilitate the translations of documents, and interpret the interviews with key persons.

⁶¹ M. Nansalma, MAS

Using this collected evidence, the next step (Aim 3) entailed a retrospective analysis of the interactions between the spread of brucellosis and the applied surveillance strategies. The analysis was qualitative and quantitative. The qualitative analysis assessed the surveillance policies along the elements of best practice to point out policy gaps. The quantitative analysis identified policy gaps and merged applied surveillance policies with the epidemiology of the spread of disease. This was carried out using whole SR flock vaccination campaign (1975 – 1985) data: the effectiveness of the vaccination campaign was evaluated with the SIR-model, producing important results. Multiple regression analysis was applied to analyse the significance of the disease reservoirs of the different animals on the infection in humans. Knowledge on the animal-human transmission was needed to evaluate the efficacy of surveillance policies. New insights on the data quality and related policy implications have now been provided.

The last step (Aim 4) called for an overall assessment to sum up the “lessons learned” from which to formulate policy recommendations about future brucellosis surveillance policies in Mongolia.

This final chapter includes five elements: (i) a discussion on the limitations and contribution of this thesis; (ii) a review of major lessons learned, (iii) a discussion of their validity; (iv) policy recommendations for future brucellosis control in Mongolia, and (v) a short outlook for future brucellosis control policy in Mongolia.

2. Discussion of the methodology

Methodological difficulties

Data collection

Language barrier

The language barrier was an important issue for the data search in Mongolia as it was difficult, time-consuming and costly to search, identify and translate scientific papers and policy documents in Mongolia. However, research partners assisting the author in this work established a high level of data quality and consistency which minimised potential bias.

Difficulties in accessing information

There were difficulties in tracing the surveillance policies dating from the era of centrally planned economy, as the archives within the MoH and MoA contained only documents from 1991 onwards. With help of the key informants it was possible to get very precise information on missing documents that was needed to find them in the Central Governmental Archive (CGA). As this archive had strictly limited access, the research partners were vital.

Data quality

Review of the dataset indicated concerns about the way the data had been compiled. Errors were found, for example, in data for cattle in the years 1987 and 1988 in some Aimags (*see chapter 4*): the data obtained from active surveillance had been mixed with reported data. It was shown that the regularly reported prevalence rates might have been topped up with data from surveillance activities.

A further problem arose concerning the epizootiological entities: the data on animal prevalence represented the infected individual animals, but the epizootiological entity in brucellosis surveillance should be the animal herd rather than the individual animal (*see chapter 2*). However, in nomadic livestock breeding conditions, animals

roaming an extended area such as an Aimag could easily have been considered as a single herd entity from the surveillance point of view (*see chapter 4*).

Analysis

Qualitative analysis:

The surveillance policy has been analysed against the basic steps required for a surveillance system according to best practice (*see chapter 6.1.*). However, the policy documents contained orders and plans for surveillance, but not details of the activities finally implemented. It turned out that there were only few evaluation activities giving information on the actual implementation. These details could only be obtained through interviews with key persons and personal observations.

Quantitative analysis:

A SIR-model has been applied to compute the host – parasite population dynamic (*see chapter 6.2.*). This is a strictly deterministic model, which does not consider random events, such as geographical distribution of the disease occurrence or demographic dependence. The model used time steps of one year, but could become smoother by reducing the time steps to half-year or quarter-year intervals (*Zinsstag J. et al, 2005a*). Stochastic events, spatial dependencies between neighbouring Aimags and different sample sizes, could be considered using a Bayesian model (*Staubach C et al, 2002*).

Fitting the demographic parameters to the real data considered three different time periods according to fundamental changes in the course of time influencing the animal populations' records. However, for fitting the transmission rate to the real data of the susceptible and infected SR, a time period with no disease control activities had to be used to observe the natural spread of disease (*see chapter 6.2.*). The only time slot was after the end of the T&S campaign in 1968, and before the immunisation campaign from 1975 gradually onwards. Potential changes of the natural transmission rate over time could not be considered because of interference coming from permanent disease control activities. The initial values applied for the mathematical

fitting process (*see table 6.1., chapter 6.2.*) were based on previous work (Zinsstag *J. et al*, 2005a). The efficacy of the Rev.1 vaccine was set at 65%, as in prior studies, though literature reported higher potential efficacy of Rev.1 up to 95% (Zinsstag *J. et al*, 2005a). This led to a higher critical vaccination level for eradication, but considered local conditions such as losses due to poor cold-chain deficiency. The analysis was done at the example of data out of 8 Aimags, chosen as they were the first included in the vaccination campaign. However, the southern and eastern parts of Mongolia were underrepresented because of this (*see figure 6.4. & 6.5., chapter 6.2.*) but the results of the analysed Aimags fell within a narrow range, therefore it was not expected to get new insights by adding further Aimags into the analysis.

We used negative binomial regression analysis, rather than the usual Poisson regression for incidence rates, to take into account the large degree of variation in human incidence rates (*see chapter 6.2.*). The logit transformation was applied to the animal prevalence to make the relation with human incidence more linear. The analysis did not consider spatio-temporal effects, as the association was highly significant ($P\text{-value} < 0.0001$), and we did not expect a spatial/temporal analysis would influence the results (*see chapter 6.2.*). Suspected heterogeneity in the data collection, which may have possessed a limiting factor to the validity of the analysis, had only been confirmed with prevalence rates of cattle in 11 Aimags in the years 1987 and 1988. Thus this was an infinitesimal part of the data and did not affect the analysis.

Contribution

This thesis presently addresses gaps in the knowledge of brucellosis and its control on various levels, which are outlined below.

Contribution to current discussion in Veterinary Public Health

In the current discussion on the role of Veterinary Public Health⁶² (VPH) for controlling zoonotic diseases in developing countries it has been realised that successes of brucellosis control programmes in the past were variable. The development of improved vaccines and tests may have been over-emphasised, while on the other hand, epidemiology may have been ignored as a basic means of control (*Robinson A, 2003b*). “More attention should be given to monitoring key indicators of disease status.....as well as on the collection of information to determine the effectiveness of specific interventions. Analysis of local surveillance data gives valuable insights into the epidemiology of the disease within the country” (Dr. Jackson in (*Robinson A, 2003b*)). It has been recognised, that there is a gap in data collection and data analysis in VPH programmes in developing countries, and this thesis addresses it and thus directs future efforts of brucellosis control to achieve greater effects.

Data collection and analysis

Applying diverse methods of triangulation (*see chapter 3*) assured a high quality data and facilitated the qualitative and quantitative analysis.

We were able to trace policy documents that were sufficiently close-meshed to get a comprehensive picture, even though some of the official policy papers could not be found (*see chapter 5*). This allowed a qualitative analysis, based on best practice, to identify potential policy gaps. This “best practice” has been defined from the general literature on epidemiological surveillance policies, as well as from specific literature on brucellosis surveillance policy (*see chapter 6.1.*).

It showed that despite the limitations expressed for the data quality (*see chapter 4*), clear results could be generated in the quantitative analysis. The data was sound enough for the mathematical modelling of the birth and mortality rates in SR and the

⁶² At the Teramo (Italy) conference (1999), held on the contribution of VPH programmes to human health, the consensus definition of VPH was: “The contribution to the physical, mental and social well being of humans through an understanding and application of veterinary science”. (*Robinson A, 2003b*)

transmission rate between SR. Furthermore, the multiple regression analysis on animal human transmission produced clear results.

The mathematical analysis aimed to calculate the critical vaccination level for eradication, and to compare it with the current vaccination policy. To fit the transmission rate between SR, the *SIR-Model* was applied, which has been modified in recent work for analysing brucellosis transmission in Mongolia (*Roth F. et al, 2003*) (*Zinsstag J. et al, 2005a*). This thesis has therefore validated the brucellosis transmission model by applying more comprehensive data. It showed that this model could be applied to other contexts of brucellosis transmission.

Contribution to the discussion on the “one health” approach

Simultaneous epidemiological studies on public and animal health were conducted. This provided the opportunity to assess their epidemiological link, and to emphasise the importance of institutionalised interaction between public health and veterinary authorities. The “one health”⁶³ approach involves closer interaction between human and animal health systems which has to be addressed with the implementation of disease control policies in a nomadic setting. “A “one health” perspective enhances zoonoses detection and control by intersectoral surveillance and communication” (*Zinsstag J. et al, 2005b*).

Research partnership

The research partnership with M. Nansalma and the MAS facilitated contacts with Mongolian institutions, and surmounting the language barrier. However, there were other far reaching and important benefits from this research partnership. It opened access to vulnerable, marginalised populations in remote areas in Khuvsgul Aimag,

⁶³ The term “one medicine” has been coined by Calvin Schwabe in the 1960s (*Schwabe C W, 1984*), focusing on the similar interests of human and veterinary health, and showing that the added value to public health of this approach could not be achieved by the disciplinary approaches alone. In the 1980s this concept evolved to the “one health” approach, containing health to the whole ecosystem (*Zinsstag J. et al, 2005b*).

and allowed us to understand their specific problems concerning brucellosis. Detailed insights were obtained concerning limited access to diagnosis and healthcare, or critical neglect in the implementation of the current vaccination campaign, threatening its effectiveness. The research partnership helped to ensure the validity of the collected data and observations and provided therefore a strong foundation for making evidence based policy recommendations.

A further benefit of this research partnership is that the Mongolian experiences, and scientific results obtained during brucellosis control, are now accessible to the English speaking scientific world through the work described herein and through publications (*Roth F. et al, 2001*) (*Zinsstag J. et al, 2005a*) (*Roth F. et al, 2006*).

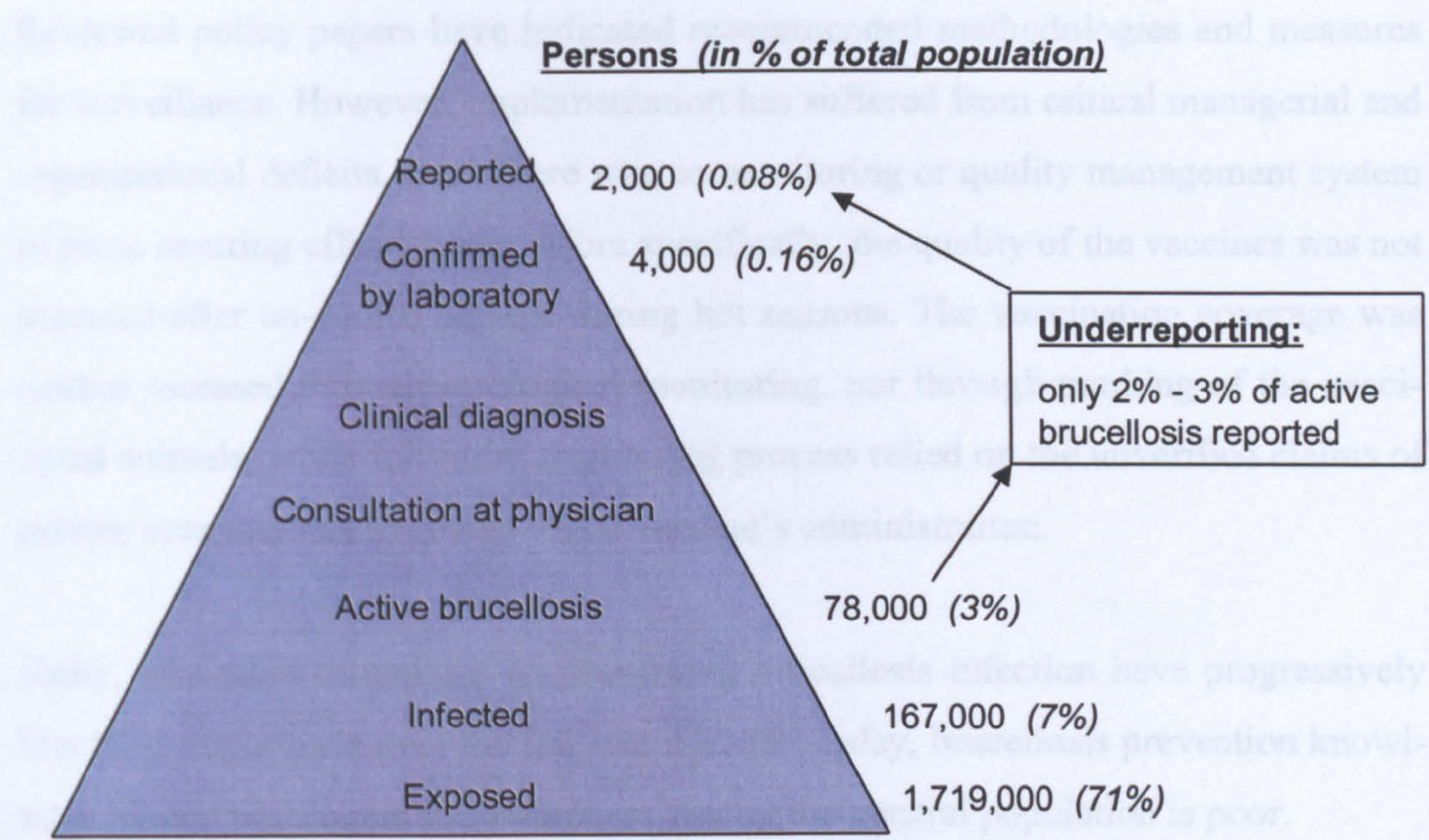
3. Main findings

Underreporting of human brucellosis

The etiological analysis concluded that brucellosis infection in humans was mainly due to *B. melitensis* and that the animal reservoir for human infection was for the most part in SR (*see chapter 4*). The determined route of infection was animal contact, thus human infections had work related causes. The statistical analysis, however, showed that the registered human brucellosis cases were related to infections in cattle and not SR. The author concludes that the registered cases are not the high risk population – i.e. pastoralist working with SR in nomadic settings, but the urban population living closer to health care facilities, mostly infected through contaminated cow's milk or through contact in dairy farms (*see chapter 6.2.*).

If this is a reality, then it ensues that there could be much under-reporting of human brucellosis, as illustrated in *figure 7.1* showing under-reporting estimates of the year 2000. Detailed calculation leading to these figures is given in *appendix 7.1.*

Figure 7.1.: Under-reporting of human brucellosis in Mongolia (2000)



Derived from material collected for this thesis

Approximately 78,000 persons were considered to suffer from active brucellosis, while only 992 new cases of human brucellosis have been reported (2000⁶⁴), leading to approximately 2000 registered brucellosis patients. This meant that only 2%-3% of all patients with active brucellosis have been serologically diagnosed and got appropriate treatment. The public health significance of human brucellosis is underestimated in Mongolia.

Missing analysis, monitoring and dissemination

The assessment of the surveillance policy papers showed that regular data analysis has been mostly missing (*see chapter 6.1*). This has had an historically critical impact on evaluation, as conclusions could not be drawn from the evidence assembled

⁶⁴ Mongolia published one of the world's highest incidence rate for human brucellosis: 41.7/100,000 in 2000 (*see chapter 2*).

over years of control work. Unfortunately, Mongolian scientific papers did not undertake this important analysis either, only expanding on the qualitative data.

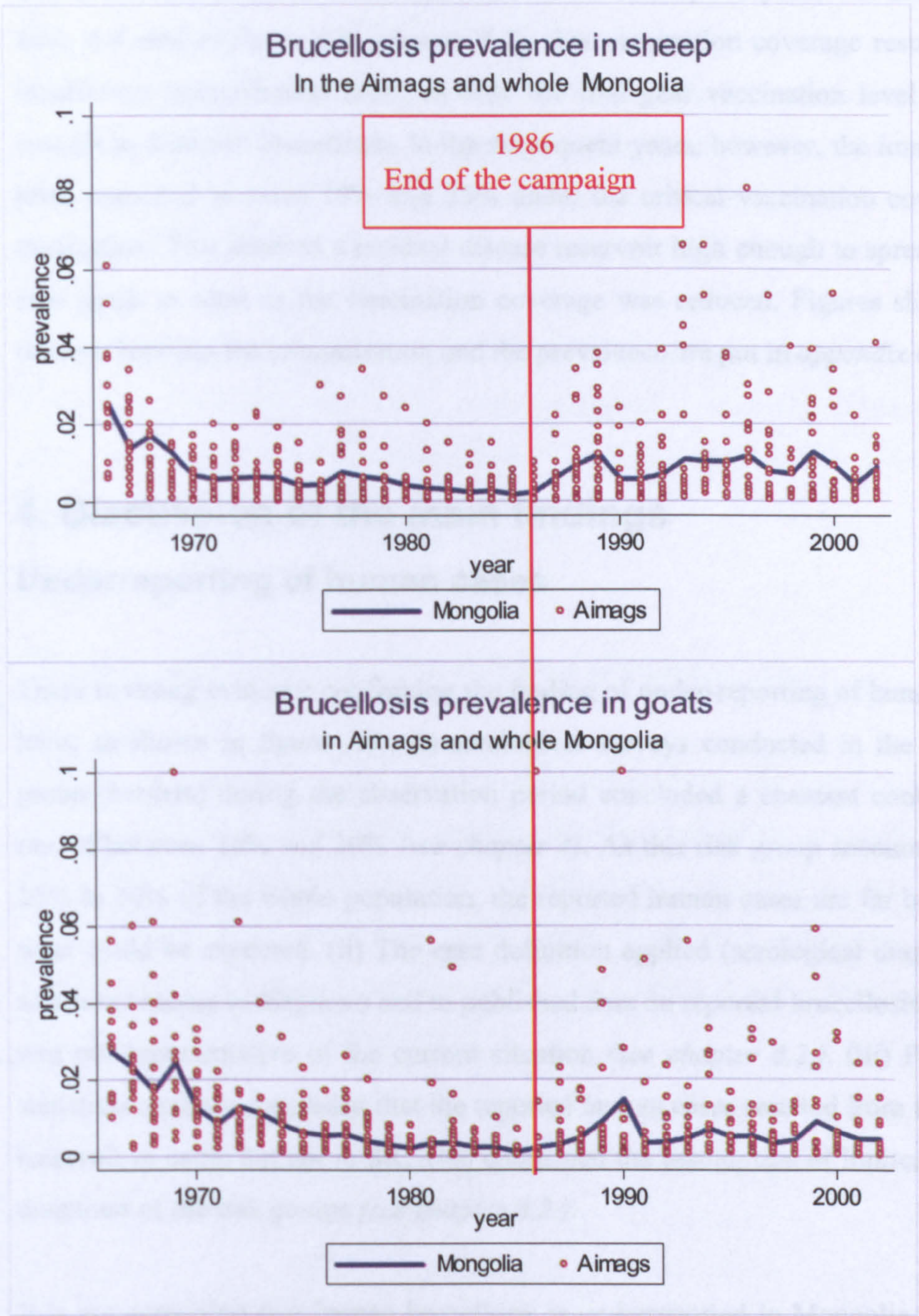
Reviewed policy papers have indicated recommended methodologies and measures for surveillance. However, implementation has suffered from critical managerial and organisational deficits, since there was no monitoring or quality management system in place assuring effectiveness. More specifically, the quality of the vaccines was not assessed after un-cooled storage during hot seasons. The vaccination coverage was neither assessed through serological monitoring, nor through marking of the vaccinated animals, while the entire monitoring process relied on the unverified claims of private veterinarians in charge of the vaccine's administration.

Sadly, education campaigns on preventing brucellosis infection have progressively lost their importance over the last two decades; today, brucellosis prevention knowledge among physicians and awareness among the general population is poor.

Insufficient animal immunisation

The Mongolian vaccination campaign 1975 to 1985 was considered, worldwide, as one of the most successful large-scale immunisation programmes employing Rev.1 to vaccinate SR (*Elberg S., 1996*). The decline of the incidence rate in humans and the reduction of the abortion rate in SR encouraged this view. However, as documented by the analysis briefly summarised below, prevalence rates in SR increased again demonstrably as soon as the vaccination campaign stopped in 1986 (*see figure 7.2.*).

Figure 7.2.: Increasing brucellosis prevalence in sheep and goats after termination of vaccination campaign in 1986



Derived from material collected for this thesis

The mathematical analysis showed that the proportion of vaccinated animals was insufficient to bring about the disease's eradication. The vaccination scheme con-

ducted whole herd vaccinations during the first year of the campaign, and immunised only newborn animals during the subsequent years. The average vaccination rate in the first year was 76%, and 26% in the subsequent years. As illustrated in *table 6.4.* and in *figure 6.6 (chapter 6.2)*, this vaccination coverage resulted in an insufficient immunisation level, as only the first year vaccination level was high enough to diminish brucellosis. In the subsequent years, however, the immunisation level remained between 15% and 35% under the critical vaccination coverage for eradication. This allowed a residual disease reservoir high enough to spread the disease again as soon as the vaccination coverage was reduced. Figures showing the relation between the immunisation and the prevalence are put in *appendix 6.4.*

4. Discussion of the main findings

Underreporting of human cases

There is strong evidence confirming the finding of under-reporting of human brucellosis, as shown in *figure 7.1.*: (i) serological surveys conducted in the main risk group (herders) during the observation period concluded a constant contamination rate of between 16% and 30% (*see chapter 4*). As this risk group account for about 25% to 30% of the whole population, the reported human cases are far below from what could be expected. (ii) The case definition applied (serological diagnosis) led to limited access to diagnosis and to published data on reported brucellosis cases that was not representative of the current situation (*see chapter 6.2.*). (iii) Finally, the statistical analysis concluded that the reported human cases resulted from the disease reservoir in cattle but not in SR. This confirmed the assumption of limited access to diagnosis of the risk groups (*see chapter 6.2.*).

It is not surprising that human brucellosis is underreported in Mongolia, as human brucellosis is underreported worldwide, remembering the reporting rates in France of 20%, in Spain of 8%, in the USA of 3.5%, and in developing countries even less (*see chapter 1*). However, the situation in Mongolia is different, as the underreport-

ing is based on one of the highest reporting level worldwide (*see chapter 2, figures 2.1.d, and figure 2.2.*).

The applied case definition, together with the current situation of not providing serological testing on Soum level, acts like a “filter of perception” for the authorities. The author concludes, based on previous work, that the health authorities are not aware on the real extent of brucellosis contamination in humans, and that the public health significance of human brucellosis is underestimated in Mongolia.

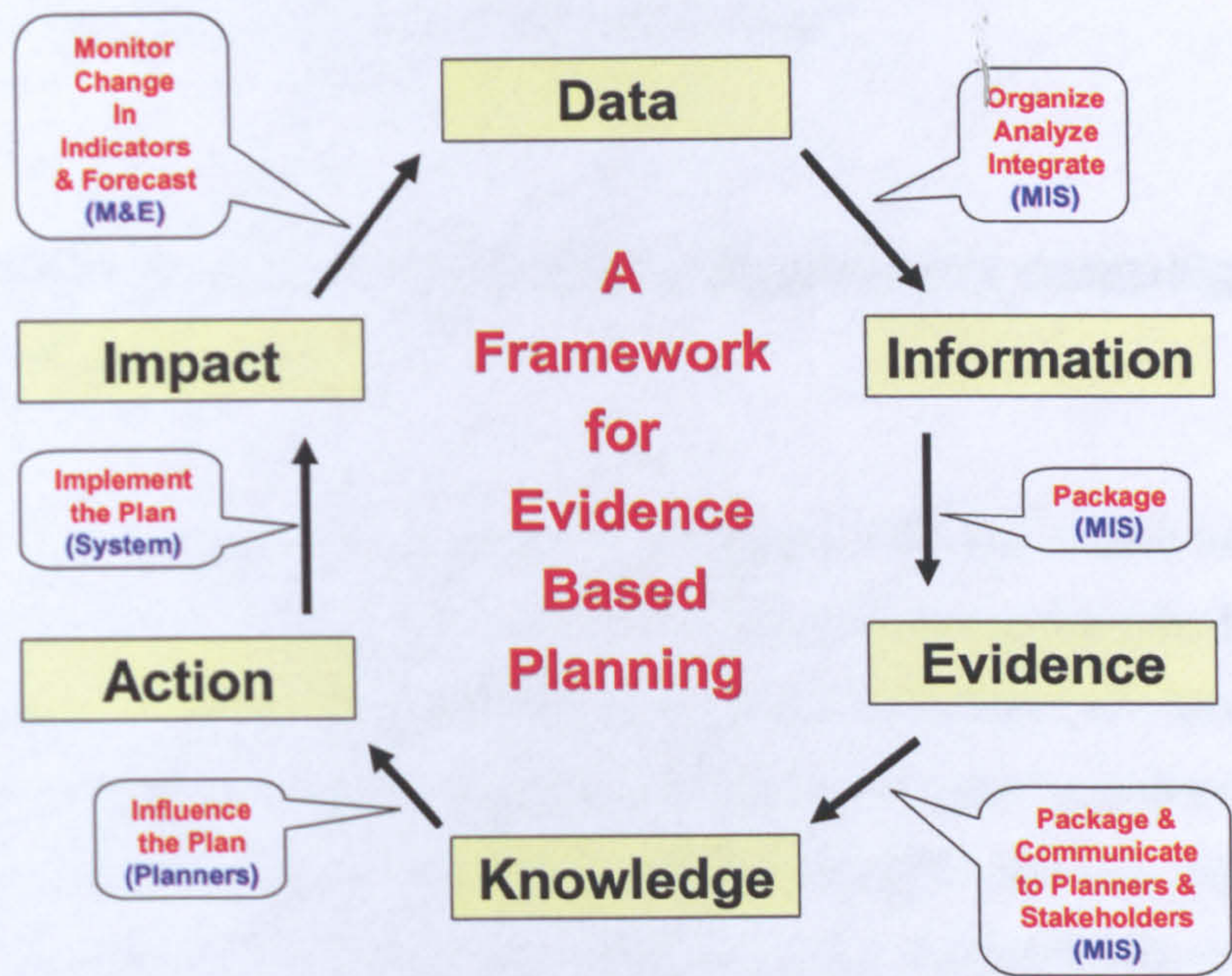
Considering the underreporting due to limited access to diagnosis, the recent variations in the incidence rate ⁶⁵ may mirror variations in access to diagnosis and not variations in the spread of disease itself. The underreporting may therefore mask future success or failure of disease control activities.

Missing analysis, monitoring and dissemination

Literature on monitoring future impact of disease burden in developing countries calls for situating monitoring and evaluation more strategically in a framework leading to a pathway for evidence based decision-making (*see figure 7.3.*): “...there is often confusion in the use of terms such as data, information, monitoring, evaluation, and forecasting, and how these conceptually fit together in management information systems.” (*De Savigny D. et al, 2004*).

⁶⁵ Reported human brucellosis cases: 685 (2001); 652 (2002); 751 (2003); 634 (2004); 836 (2005) (*derived from material collected for this thesis*)

Figure 7. 3.: A pathway for evidence-based planning



M&E = monitoring and evaluation;
MIS = management of information system
(De Savigny D. et al, 2004)

Crucial in this concept is that often a short-circuit was observed going directly from “Information” to “Action”, without considering distilling the information to evidence, packaging the information, and communicating the evidence to the stakeholders to transform to new knowledge or new understanding on the next steps. In Mongolia it was observed that there was a short-circuit between “Data” and “Action” (see figure 7.3.). The policy analysis resulted that the data were aggregated and tabulated, but not analysed, and not interpreted for the specific information needed for surveillance practice. This resulted in a weak information system. From 1980s onwards, the policy papers didn’t include frameworks for capacity building. As a consequence poor knowledge was frequent among stakeholders. The decision makers draw their plans for surveillance relying on “Data” but not on “Evidence”. While implementing the plans, a quality management was not in place. Finally the changes

in indicators such as the contamination in the animal reservoir or the treatment of brucellosis patients have not been monitored, resulting in underreporting. Thus, the short-circuit went back from “Action” to “Data”.

Mathematical analysis of the vaccination campaign 1975/1985

Worldwide, whole herd vaccination campaigns with Rev.1 have been - until now - the only accepted method to control *B. melitensis* among nomadic SR in developing countries (*Blasco J M, 1997*) (*Banai M, 2002*). As financial resources for large-scale compensation schemes for slaughtered animals are missing in developing countries, T&S programmes can only follow after significantly reducing disease prevalence. The success of these vaccination programmes have traditionally remained partial at best, because of the difficulties encountered, among others, in reaching every nomadic farm. In addition, the campaigns were not accompanied with bacteriological surveys, thus the evidence base required to assert the success or failure of the programmes was never established (*Banai M, 2002*).

The thesis addresses this gap with assessing the effectiveness of past immunisation campaigns. This was made possible by the new evidence base compiled in the course of this research work, and with providing an epidemiological model for analysing. Hints for the critical vaccination level for eradication needed in current and future immunisation campaigns are given. This is important, as brucellosis is affecting the well being of societies in developing countries worldwide, and the efforts for research and control have to be rethought (*Zinsstag J. et al, 2006*).

5. Policy recommendations

The development of an epidemiological surveillance cycle requires the following consecutive steps (*see chapter 6.1.*) (Krämer A. *et al*, 2003) (Teusch Steven M. *et al*, 2000):

(i) Definition of the objectives

The National Programme on “Animals’ Health” (*Ministry of Agriculture, 1999*) declared in 1999 to eradicate brucellosis in Mongolia by 2010. For this a whole herd immunisation programme has been implemented in 2001, with a vaccination scheme providing higher vaccination coverage than in 1975/1985. The Mongolian Government, earmarking the funds for this vaccination campaign, seemed to be strongly dedicated to this aim of brucellosis eradication.

Recommendation

Serious deficits were observed in the implementation process (*see “Findings” above*), leading to doubts if this objective could be reached. A rigorous and prompt quality management and vaccination monitoring would be necessary to make the turn around.

(ii) Case definition

The case definition of WHO has been applied to this point in Mongolia, without considering that the rural health facilities were not able to perform serological diagnoses of brucellosis (*see chapter 6.1.*) They remained therefore not adequately responsive to the needs of the population they served. This led to limited access of the population at risk (herders) to diagnosis and treatment (*see chapter 6.2.*), due to the geographical barriers such as lack of transport facilities or not affordable transportation costs.

Recommendation

To increase access to health care for pastoral households, the Soum Hospitals must provide proper serological diagnosis and treatment for brucellosis. This is in line with the second HSDP focusing on reforming the level of referral for rural health services (*Hill P S et al, 2006*). This programme foresees improved links between Bag Feldshers and Soum Hospitals to increase access of nomadic herding communities to health care. Therefore, the Bag Feldshers have to be included in training on brucellosis etiology, diagnosis and treatment (*see recommendation under “dissemination” further down*). The drug supply for brucellosis treatment has to be assured on Soum level.

(iii) Data collection

A surveillance system should establish a methodology and mechanism for data collection which allows for its analysis and interpretation. WHO recommends routine surveillance among high risk groups, and mandatory early case-based reporting by health providers to upper levels of the public health sector as well as to the appropriate level of the animal sector (*WHO, 1999*). The intersectoral collaboration is important as surveillance data on human infection can be a sensitive indicator of infection in animals (and vice versa). The collaboration between the MoA and MoH was a well institutionalised element in the policy papers of the Mongolian Government. Despite this fact, interviews with partners from medical department concluded that the information exchange between MoA and MoH has still to be enforced (*see chapter 6.1.*).

Recommendation

Collecting routine data include the sample testing in animals, and collecting reported human incidence. Apart from this, two problems in data collection have to be tackled: (i) the underreporting in humans (*see “case definition” above*) and (ii) the missing monitoring of the immunisation campaign (*see “evaluation” further down*).

“The surveillance activities of both public health and animal health sectors must be fully coordinated and integrated. Administrative arrangements between the two sectors must be established to facilitate immediate cross-notification of cases, as well as joint investigations.” (*WHO, 1999*). Zoonotic disease control committees should be established at national, provincial and local levels, and should be multidisciplinary, including physicians, veterinarians, epidemiologists, from MoA and MoH, as well as NGOs and community representation (*Robinson A, 2003b*). Beside information exchange synergies have to be created to attempt to serve needs on human and animal health simultaneously for isolated populations such as nomadic people (*see concept of “one health” above and recommendation on “implementation” further down*).

(iv) Data Analysis

A surveillance system should determine the appropriate analytical approach to data analysis, ensuring the elevation of data to the status of information. A lack of analytical approach has been observed in the Mongolian brucellosis control policy (*see chapter 6.1.*). This was assessed as one of the weakest point in the surveillance policy over most periods of time.

Recommendation

Analytical methods have to be introduced that allow the interpretation of the collected data (*see chapter 6.2.*). Before analysing, data have to be cleaned, controlled, organised and integrated with other data. Computing with epidemiological methods, integrating both animal – animal transmission and animal – human transmission, is essential to grasp the course of disease. For this funds have to be assured. The results of the analysis should provide evidence for policy, the decision-making process leading to planning of the next steps in surveillance activities.

(v) Dissemination

To ensure a proper surveillance system, decision-making authorities should be supplied with reports on health conditions, activities performed, and the actual progress in controlling the disease. Information should not only be addressed to the authorities at the central levels, but appropriate feedback should also be provided to intermediate authorities and to field operators. The current knowledge on brucellosis is poor in the population at risk and in the health sector (*see chapter 6.1.*). The dimension of underreporting the human cases prevented the decision makers to arrange the meaning of brucellosis infection according to its impact for public health.

Recommendation

To address this, adequate information concerning prevention and treatment of brucellosis should be disseminated to policy makers, physicians and the general population, aiming at the professional and the educational level, to increase brucellosis awareness and safety education.

To guarantee diagnosis and treatment on Soum level (*see first recommendation above*) the knowledge on brucellosis etiology, diagnosis and treatment has to be assured with the physicians at the Soum hospitals and with the Bag Feldshers. Besides instruction given when studying medicine, or during further medical course work, continuous training to medical staff in remote areas could be given through distance learning programmes. This could be done on paper-based continuing training material, supplemented by CDs for stand alone PC, as long as no access to the internet is available.

The population at risk also has to be informed and trained on matters concerning prevention from brucellosis infection. Information should include eating habits, occupational practices and management of livestock. In addition, the population at risk should be informed about the clinical signs of brucellosis and the urgent need to seek health advice at the Soum Hospital. This could be done through radio and television. However, as animal health services appear to have better coverage, this knowledge

on human health has also to be transmitted through the channel of veterinary services to the nomadic population (*see approach of “one health” above*).

The pupils have to be informed at school, this could be supplemented with leaflets to bring back home. Therefore the Ministry of Education has also to be involved, as school children are the group target.

(vi) Implementation

A surveillance system should ensure the implementation of activities guided by defined objectives. Plans for implementation should define methodology, governance, resources and schedule, and consider its political, legal and cultural factors. Observations on the implementation of the current vaccination campaign lead to the conclusion that the success could be seriously threaten by lack of monitoring and through deficits in the proper implementation (*see “Findings” above and chapter 6.1.*).

Recommendation

The keys for proper vaccination campaigns should be addressed to ensure efficient immunisation: (i) the vaccines should only be delivered to the veterinarians of the private sector shortly before administration, as long as storage with cooling system is not assured. (ii) The slaughter of sero-positive animals has to be implemented. (iii) The vaccinated animals have to be marked to ease prevention through hygienic methods and to facilitate monitoring. (iv) It is necessary to develop laboratory capacities on Soum level for both sectors, human and veterinary (*human: see above “case definition”*). (v) The vaccination campaign has to be monitored through serological testing, allowing the evaluation of the effectiveness of the immunisation.

Synergies in logistics between human and animal health should be sought (*see concept of “one health” above*).

(vii) Evaluation

A surveillance system has to be regularly evaluated to ensure that defined objectives are met, and to ascertain its utility and relevance to public health. The assessment of the control policy showed that the progress of surveillance activities had been described, but that because the reporting system did not provide analysis, the evaluation remained weak (*see chapter 6.1.*).

Recommendation

Therefore, to ensure successful surveillance collecting of epidemiological data and analysing the immunisation process remain indispensable.

The evaluation of the vaccination campaign 1975/85 lead to the conclusion, that the vaccination coverage in the Mongolian context should reach at least 70% (*see chapter 6.2. and "Findings" above*) to reach the critical immunisation level for brucellosis eradication, and to avoid later flare up of the disease as soon as the immunisation level is reduced. However, the needed duration of this high vaccination coverage can hardly be predicted, as it depends on results of active surveillance data.

6. Outlook for future control policy in Mongolia

The literature mentions a possible switch from immunisation to T&S policy, which is justified on economic grounds, at a prevalence rate of 2% or less (*Scientific Committee on Animal Health and Animal Welfare of the European Commission, 2001*). However, such a shift is only possible on condition that: (i) the flocks are not too big and under strict surveillance and movement control; (ii) the animals are individually identified, the veterinary service for surveillance well organised, and the laboratory testing in place; (iii) the necessary facilities and resources for replacements or com-

pensation for a considerable period are available (*Scientific Committee on Animal Health and Animal Welfare of the European Commission, 2001*).

As these requirements are not in place, such a policy shift in the Mongolian context of nomadic SR livestock breeding would have no chance of success. It could possibly be envisaged for control of brucellosis in cattle farms, isolated from the other livestock.

This implies that brucellosis surveillance for SR in a nomadic setting in Mongolia has to rely on immunisation and that this immunisation has to be implemented and monitored according to best practice.

Between the conception
And the creation
Between the emotion
And the response
Falls the Shadow

Life is very long

*Extract from
"The Hollow Men"
by T.S. Eliot (1925)*

A good concept does not release those in control from the responsibility for the outcome, and it's so hard to maintain a relentless control programme all the time.....

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Appendices

Appendix 1.1...: Definition of list A and list B diseases according to O.I.E.

“Definition of O.I.E. List A diseases:

Transmissible diseases which have the potential for very serious and rapid spread, irrespective of national borders, which are of serious socio-economic or public health consequence and which are of major importance in the international trade of animals and animal products. Reports are submitted to the O.I.E. as often as necessary to comply with Articles 1.2.0.2. and 1.2.0.3. of the international Animal Health Code.

Definition of O.I.E. List B diseases:

Transmissible diseases which are considered to be of socio-economic and/or public health importance within countries and which are significant in the international trade of animals and animal products. Reports are normally submitted once a year, although more frequent reporting may in some cases be necessary to comply with Articles 1.2.0.2. and 1.2.0.3 of the International Animal Health code.”

Cited from: (*Office International des Epizooties, 2000*)

Appendix 1.2.: Brucellosis free countries, 1994

Countries reporting eradication of bovine brucellosis (*B. abortus*):

In Europe: Bulgaria (1968), Croatia (1965), Cyprus (1932), Czech Republic (1964), Denmark (1962), Estonia (1961), Finland (1960), Hungary (1985), Iceland (never recorded), Latvia (1963), Lithuania (1952), Luxembourg (1993), Netherlands (1993), Romania (1969), Slovak Republic (1964), Slovenia (1970), Sweden (1957), Switzerland (1963), U.K. (1993)

In Africa: Mauritius (1986)

Americas: Belize (1980), Canada (1989)

Asia: Israel (1984), Japan (1992), Jordan (1992), N Korea (1959), Papua New Guinea (1974), Philippines (1989), U.A.E. (1992)

Oceania: Australia (1989), French Polynesia (1984), New Zealand (1989), Vanuatu (1992)

Countries reporting eradication of ovine/caprine brucellosis (*B. melitensis*):

In Europe: Bulgaria (1968), Croatia (1965), Czech Republic (1964), Germany (1986), Switzerland (1963)

In Africa: Ghana (1993), Namibia (1990)

Americas: USA (1972), Chile (1987)

Asia: Cyprus (1932)

Oceania: not present

Material out of: (*1st International Conference on Emerging Zoonoses, 1997*)

Appendix 3.1.: List of interviewees

Semi-structured interviews were conducted in autumn 2003 with key persons from all the authorities responsible for the control of brucellosis in animals or in humans at three administrative levels: central level, Aimag level and Soum level. Further interviews took place with scientific experts on brucellosis, patients ill from brucellosis and herder families. For the interviews on the level of Aimag and Soum, the Aimag of *Khuvsgul* and the Soum of *Khutgul* were chosen.

The interviewees are listed in alphabetical order:

- Dr. ALTANTSETSEG, deputy Director of Public Health Organisation of Khuvsgul Aimag, interview together with Dr. NARANTSETSEG, General Epidemiologist, and Dr. BAIGAL, Physician, Clinic for Brucellosis;
- Dr. Batsukh BODIGEREL, interview together with Dr. Purevsuren BOLORTUYA, both veterinarians at the State Veterinary & Animal Breeding Department, MoA;
- Mrs. BYAMBA, Mongolian administrator at WHO local office (interview per telephone)
- Sodnom BYAMBA, Former leader of the Brucellosis vaccination at Biokombinat, now consultant at Monet Pharm Co. Lt.;
- Dr. P. CHULUUNBAATAR, former head of Brucellosis Epidemiology in the Central Veterinary Laboratory, MoA; is retired now;
- Dr. DARAATSEDER and Dr. OYUNTSETSEEG, both veterinarian of one sector of Moron, interview together with Dr. GANKHUYAG, Director of Aimag Veterinarian Office;
- Markus DUBACH, Swiss Consular and representing SDC, interview together with Ts. Enkh-AMGALAN;
- Dr. B. ENKHTUYA, Officer in charge for Communicable diseases of the Ministry of Health;
- J. ERDENECHIMEG, Epidemiologist at the NCCD (Infectious Diseases Research Centre), MoH;
- Dr. GANKHUYAG, Director of Aimag Veterinarian Office, interview together with Dr. ADUUCH, responsible for the serological laboratory in the Aimag Veterinarian Office;

- Dr. Jalkhaa KUPUL, former director of the National Institute for Hygiene, Epidemiology and Microbiology ;)
- Dr. NARANTSETSEG, General Epidemiologist, interview with brucellosis patients at the Brucellosis Department Unit, and visiting the laboratory of Moron Aimag Hospital;
- L. NARANTUYA (MD, PhD, DSc), General Director of the Public Health Institute, MoH;
- Dr. OYUNTSETSEEG, veterinarian of one sector of Moron: visiting milk and meat markets;
- Dr. Chin Y. PAK, local Program Co-ordinator Medical Mission Centre, Yonsei University Medical Centre Ulaanbaatar, interview together with GANTSETSEG, MD research student carrying out clinical research on Brucellosis;
- Dr. Reijo SALMELA, Medical Officer at WHO Representative Office in Ulaanbaatar;
- Dr. R. SODNOMDARJAA (PhD), Director of the Central Veterinary Laboratory, interview together with Dr. Ura BADAMSUREN, epidemiologist at the Central Veterinary Laboratory, MoA;
- Mrs SUKHJARGULMAA, Mongolian head of UNDP (interview per telephone),
- Dr. TSERENDOLGER, Director of Soum Hospital in Khutgul,;
- Tsedev ULZIITOGTOKH, Vice-Director Biokombinat;
- Dr. A. YONDONDORJ (Prof. Dr. PhD, Sc. D), Chief of Microbiology and Infectious Disease on Animals, Veterinary Research Institute, MoA;
- Visiting herder family in the surrounding of Moron;

Appendix 4.1.: Spread of brucellosis in Mongolia in small ruminants and humans

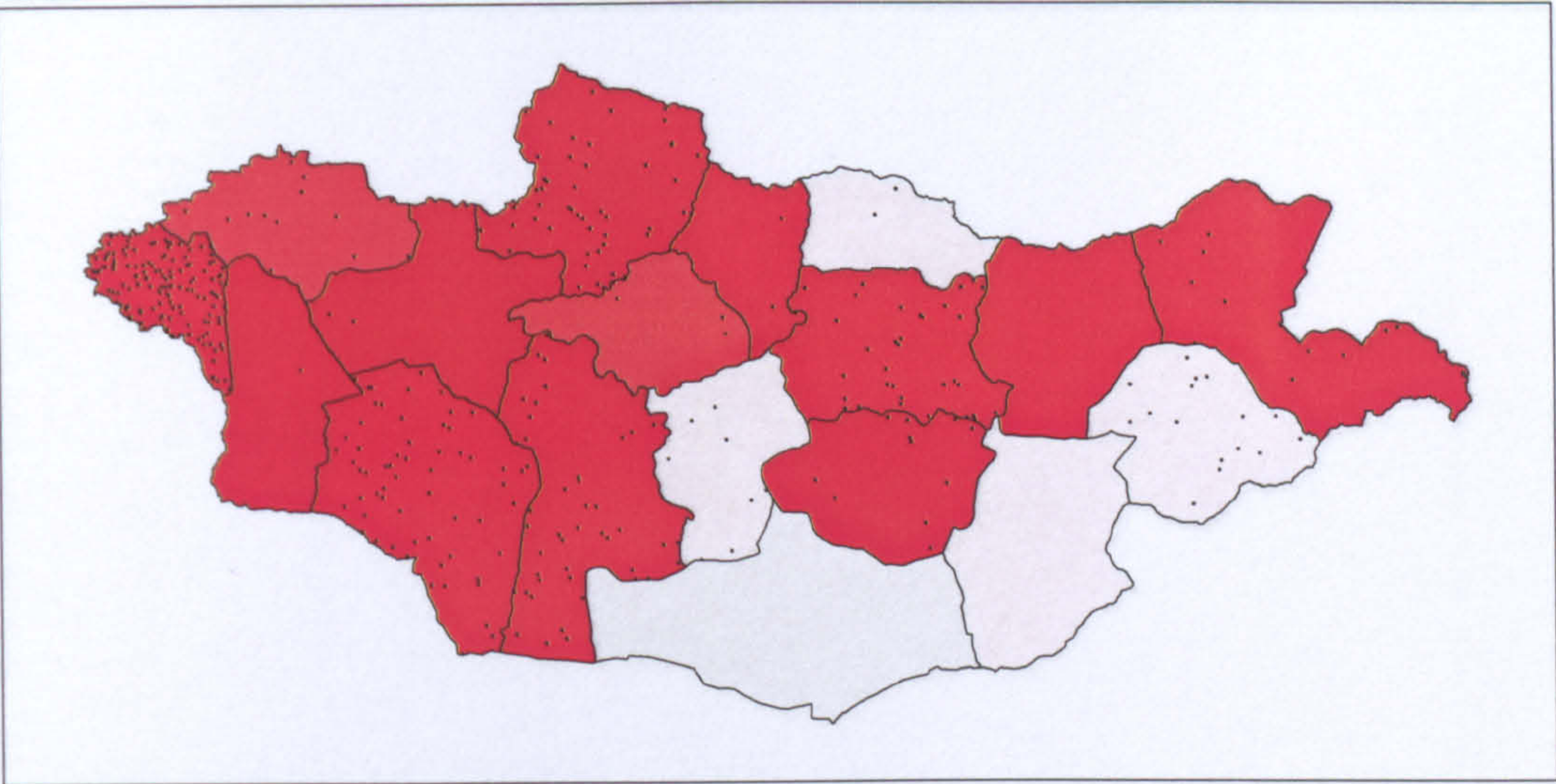
Brucellosis prevalence in SR and incidence in humans are shown with a geographical information system (*GIS Mapinfo software*). The dynamic infection and recovery processes over the whole observation period 1966 to 2002 are shown in short consecutive time slots (one year), in the manner of a film presentation. The template map of Mongolia has been downloaded from internet¹, the data are derived from material collected for this thesis (*see chapter 3*).



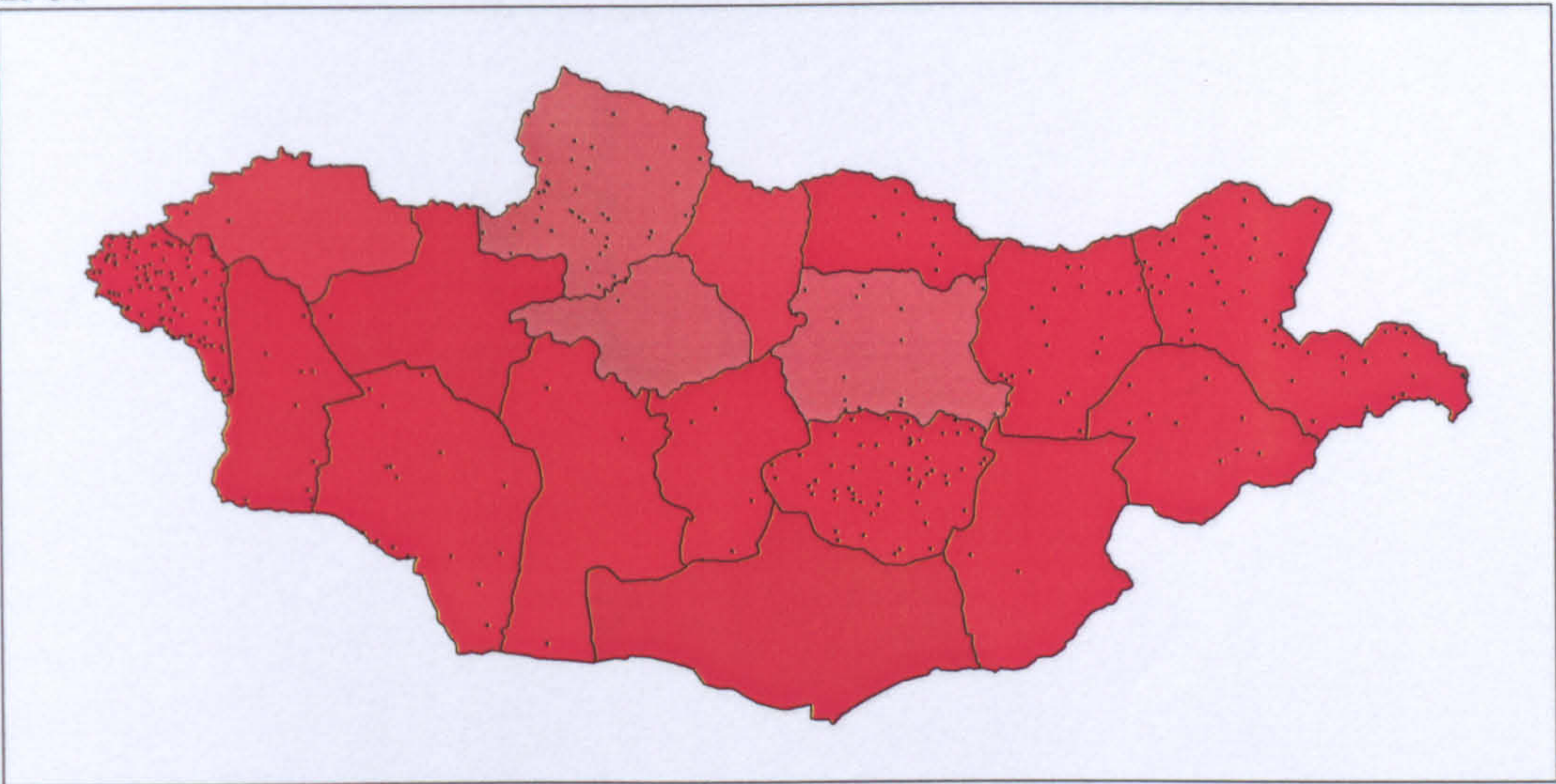
Prevalence of Brucellosis in sheep and goats <div><div><0.1%</div><div>0.1% to <0.3%</div><div>0.3% to <0.6%</div><div>0.6% to <1%</div><div>1% and more</div><div>missing value</div></div>	Incidence of Brucellosis in Humans Cases / 100'000 inh. / year <div>1 Dot = 5/100'000</div>
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¹ <http://www.cipotato.org/DIVA/data/DataServer.htm>

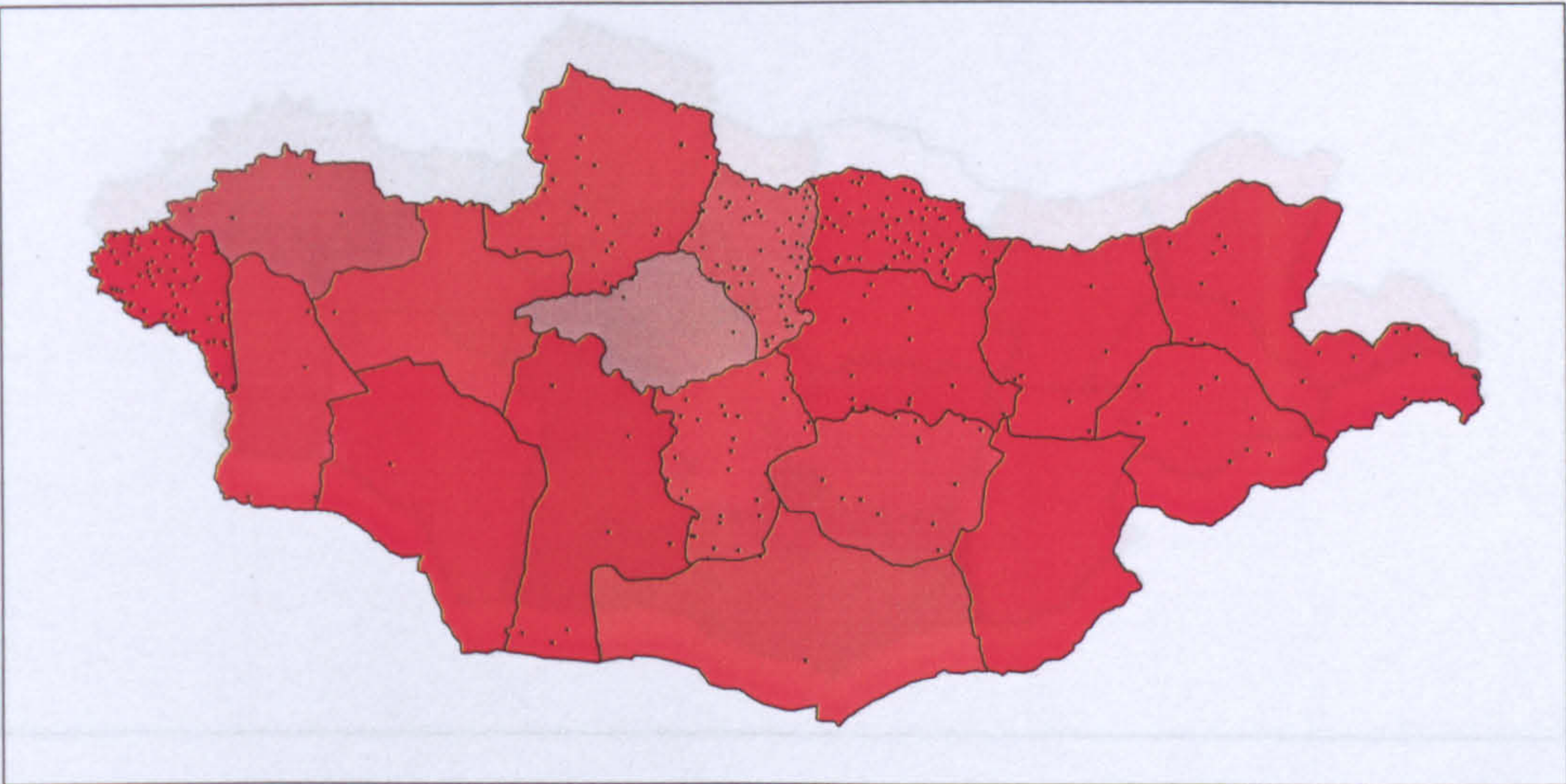
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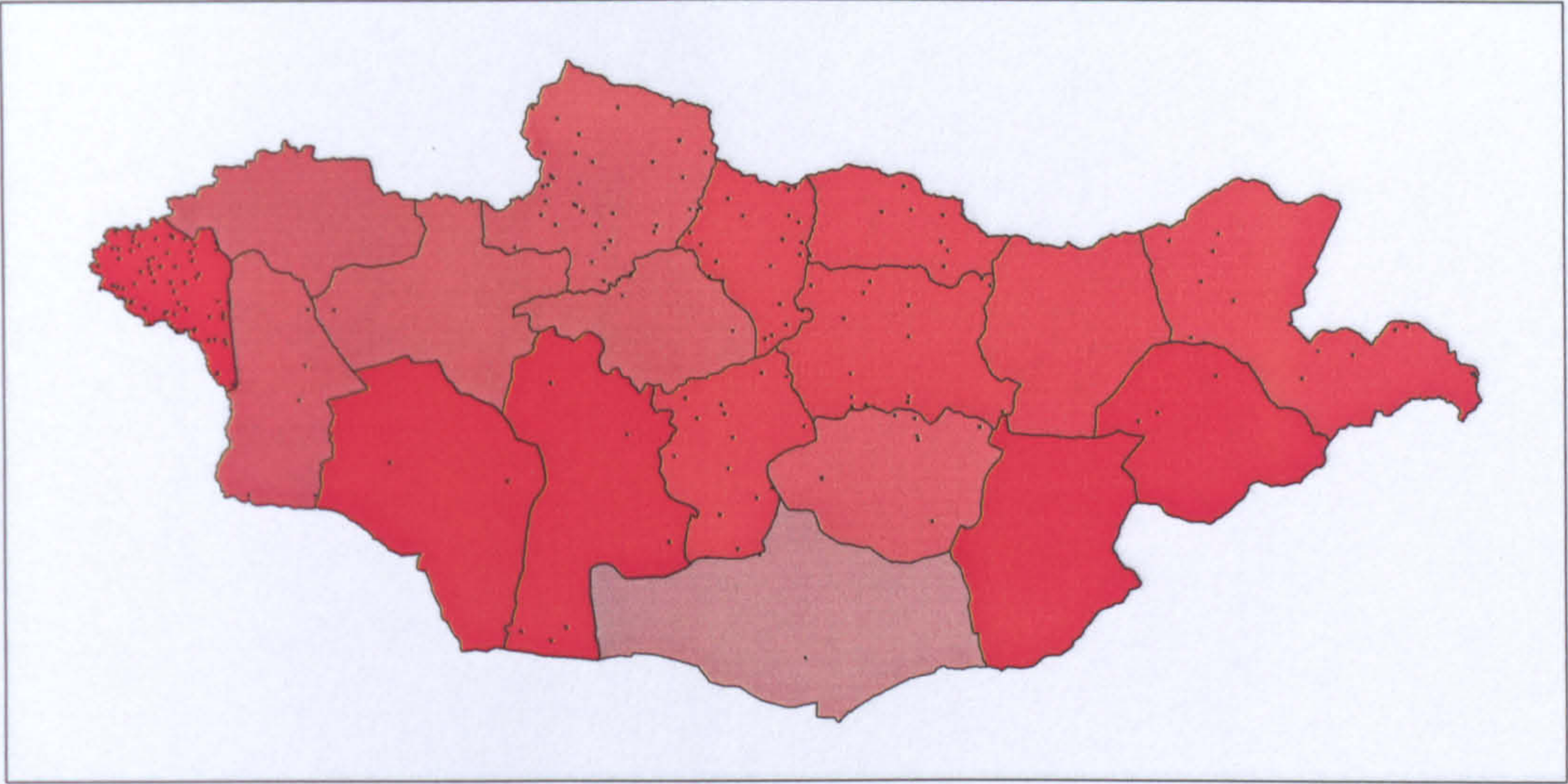
1967



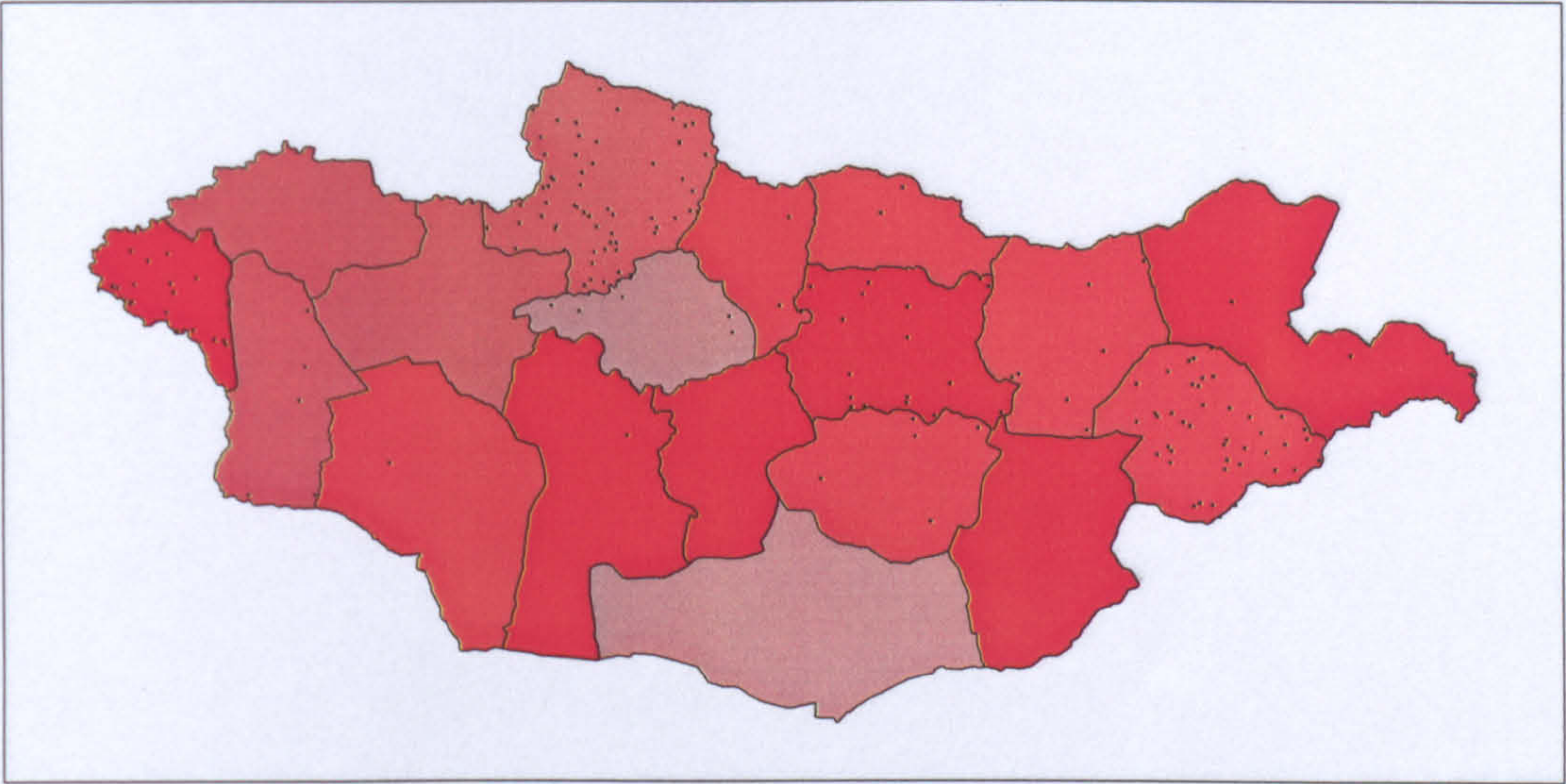
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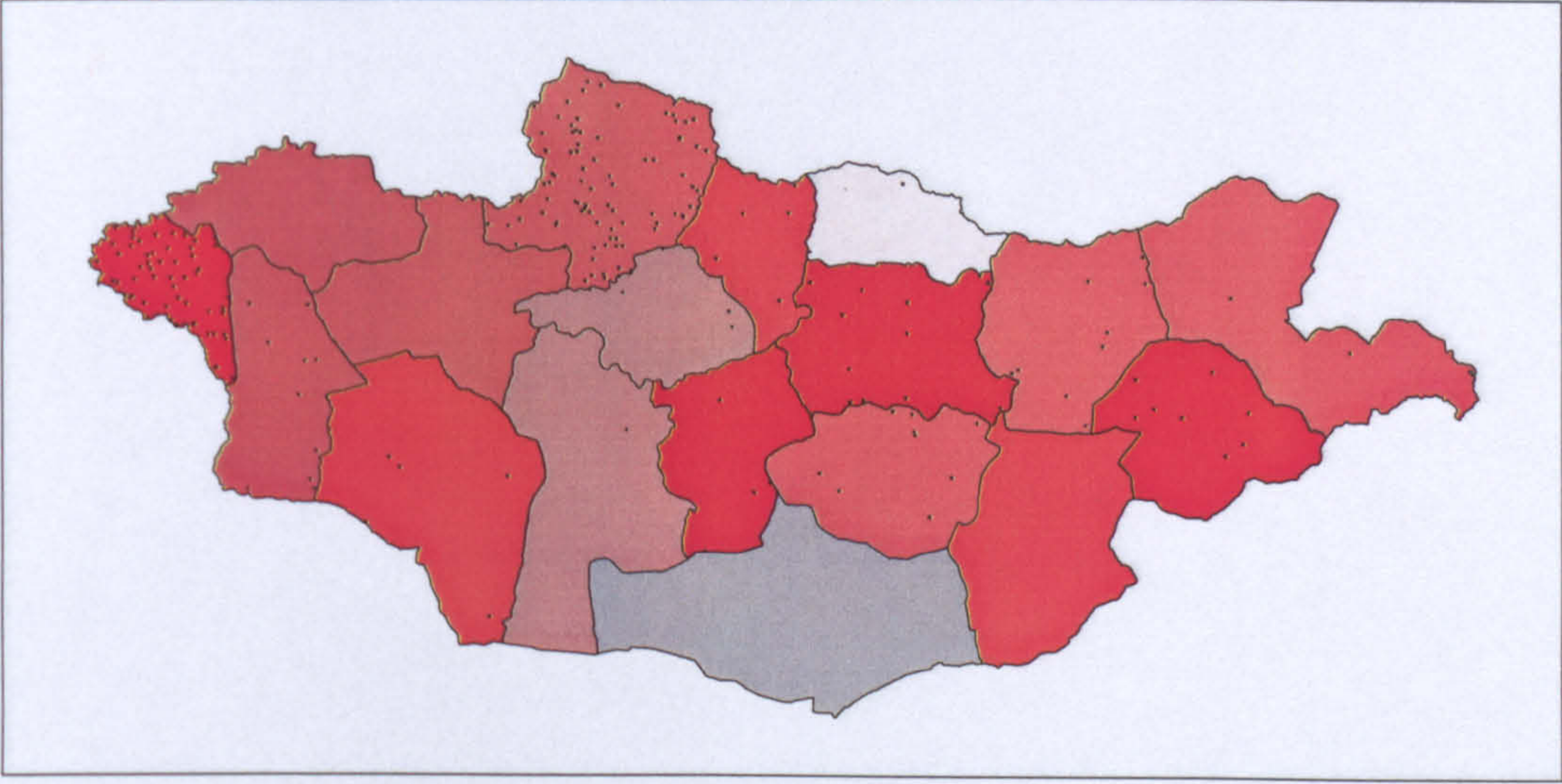
1969



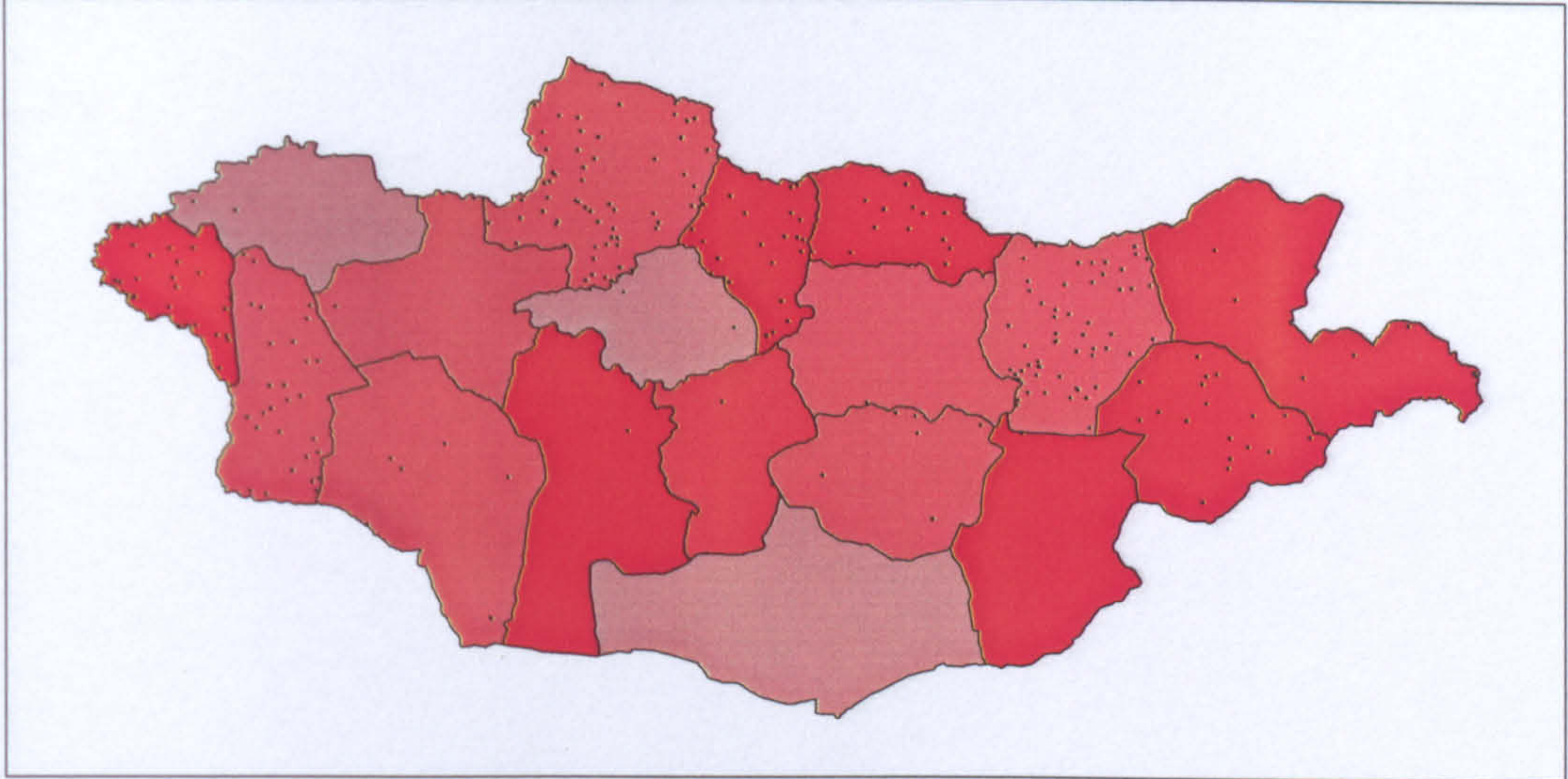
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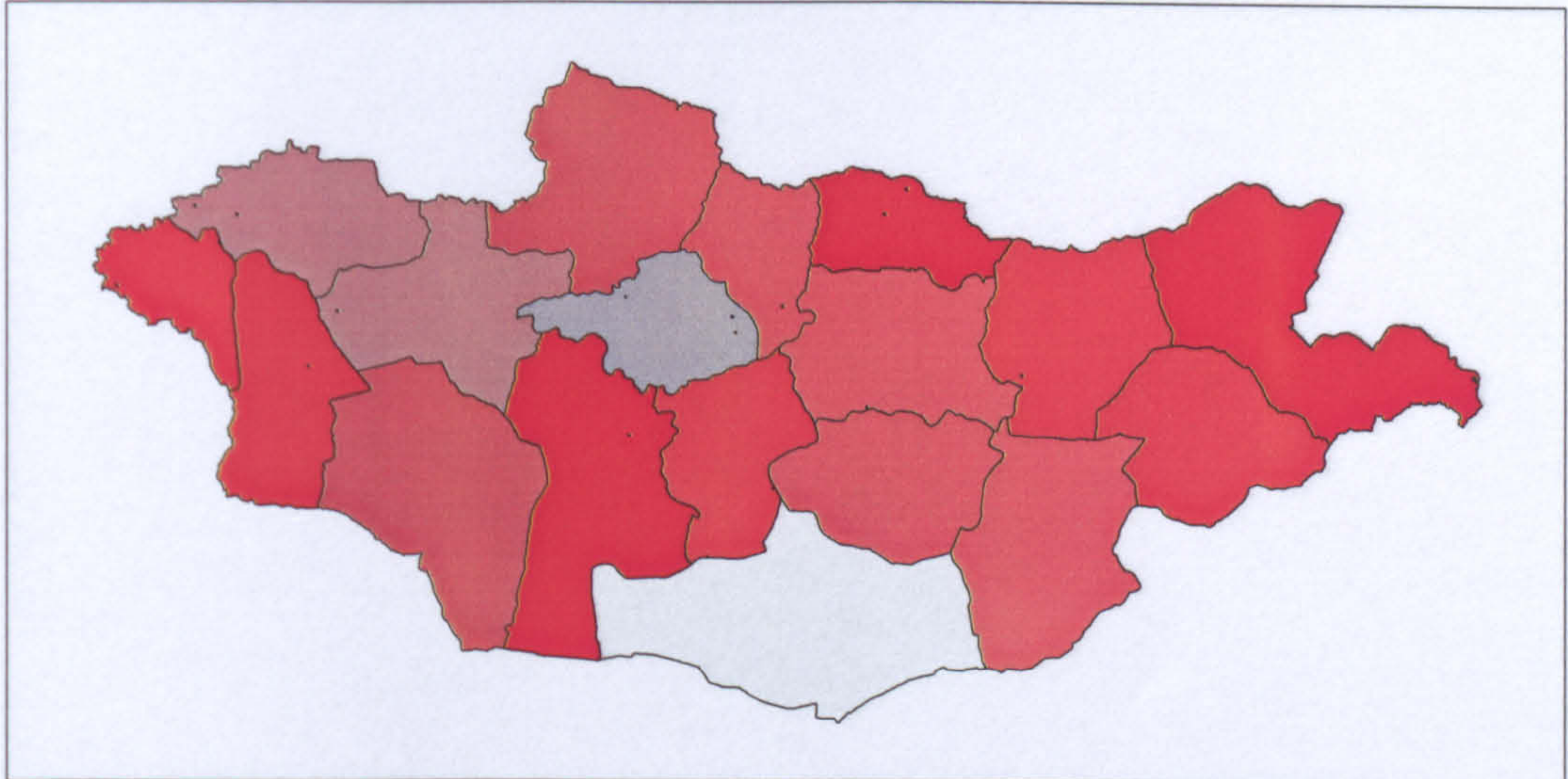
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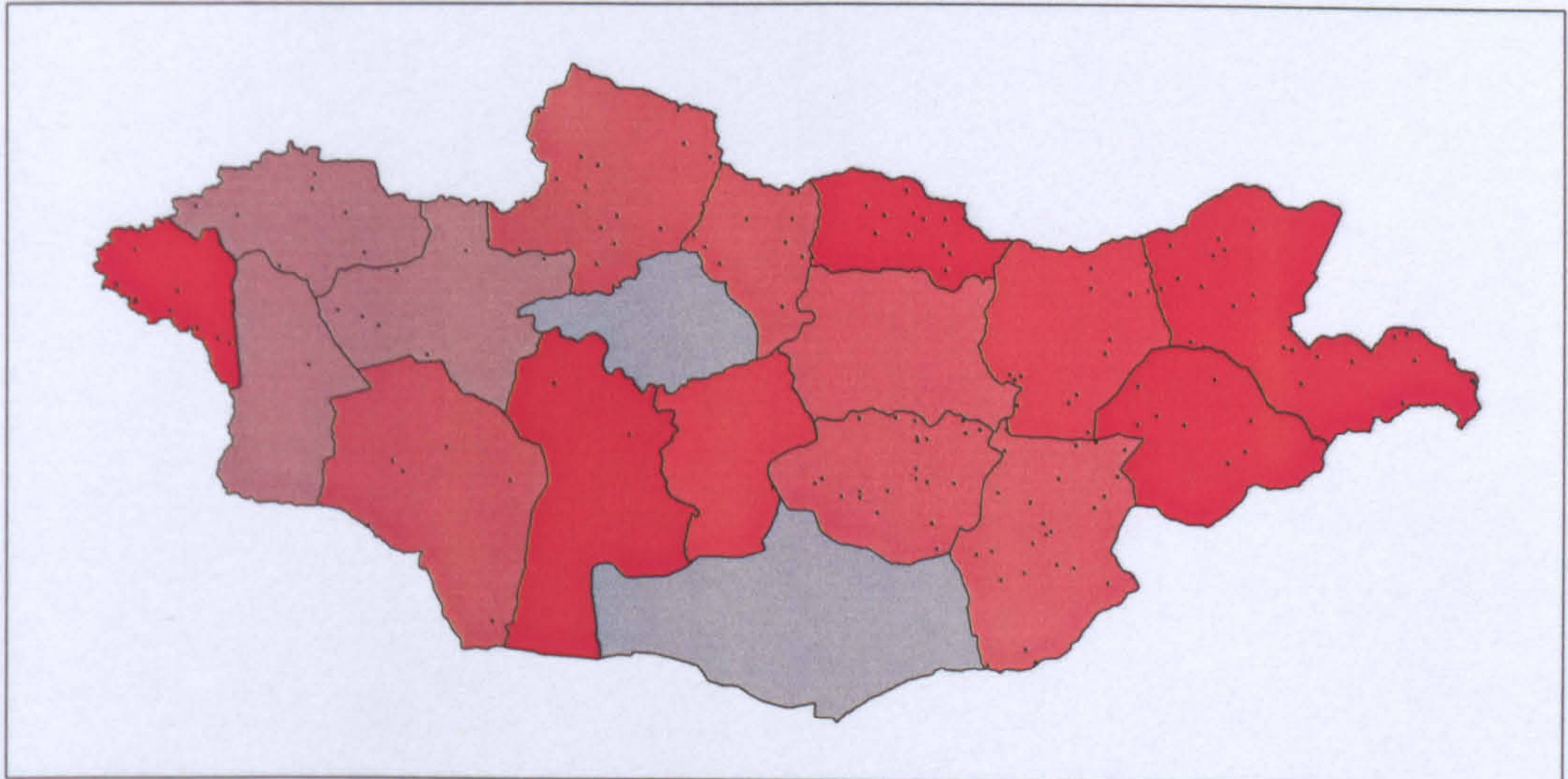
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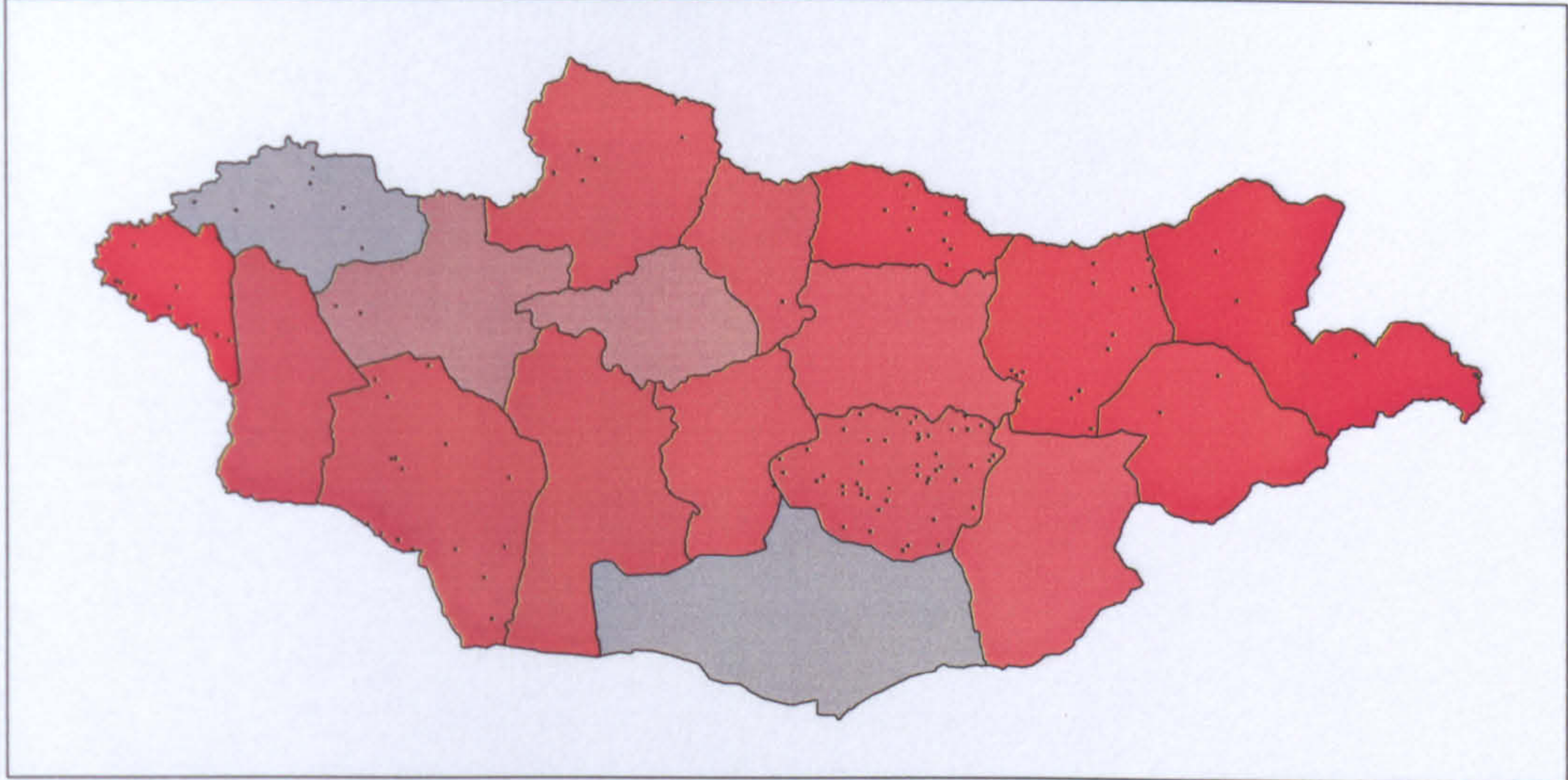
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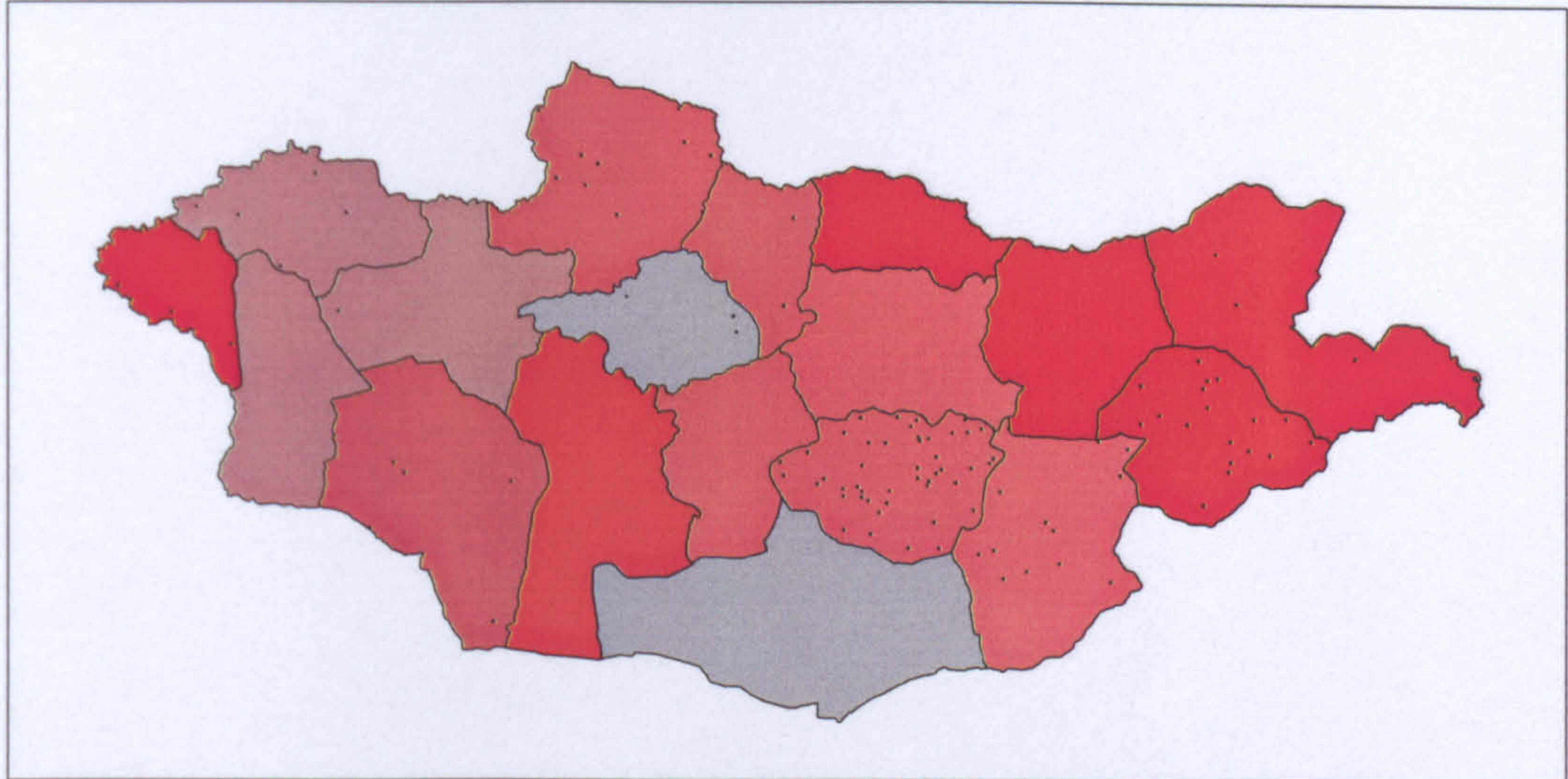
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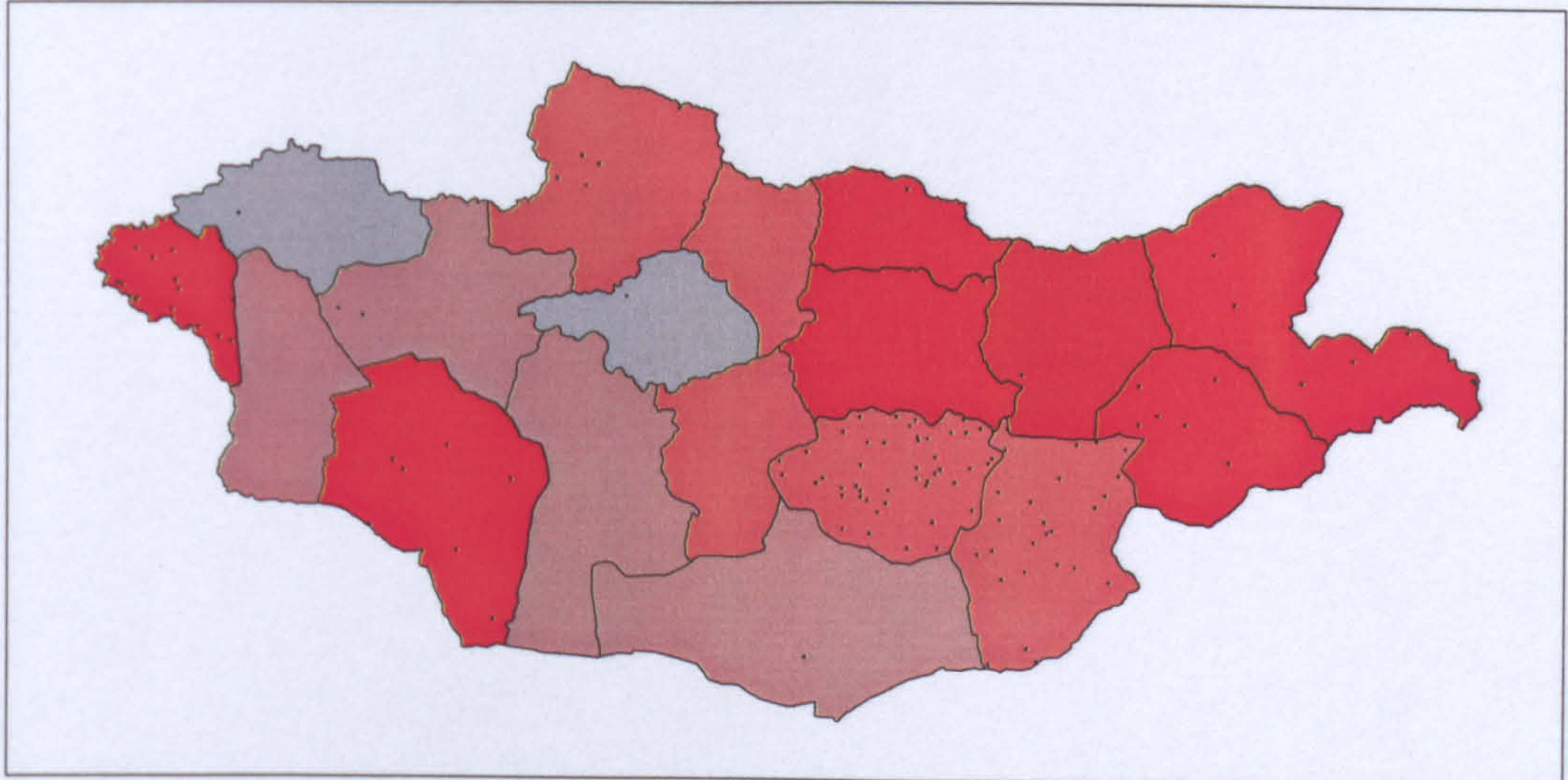
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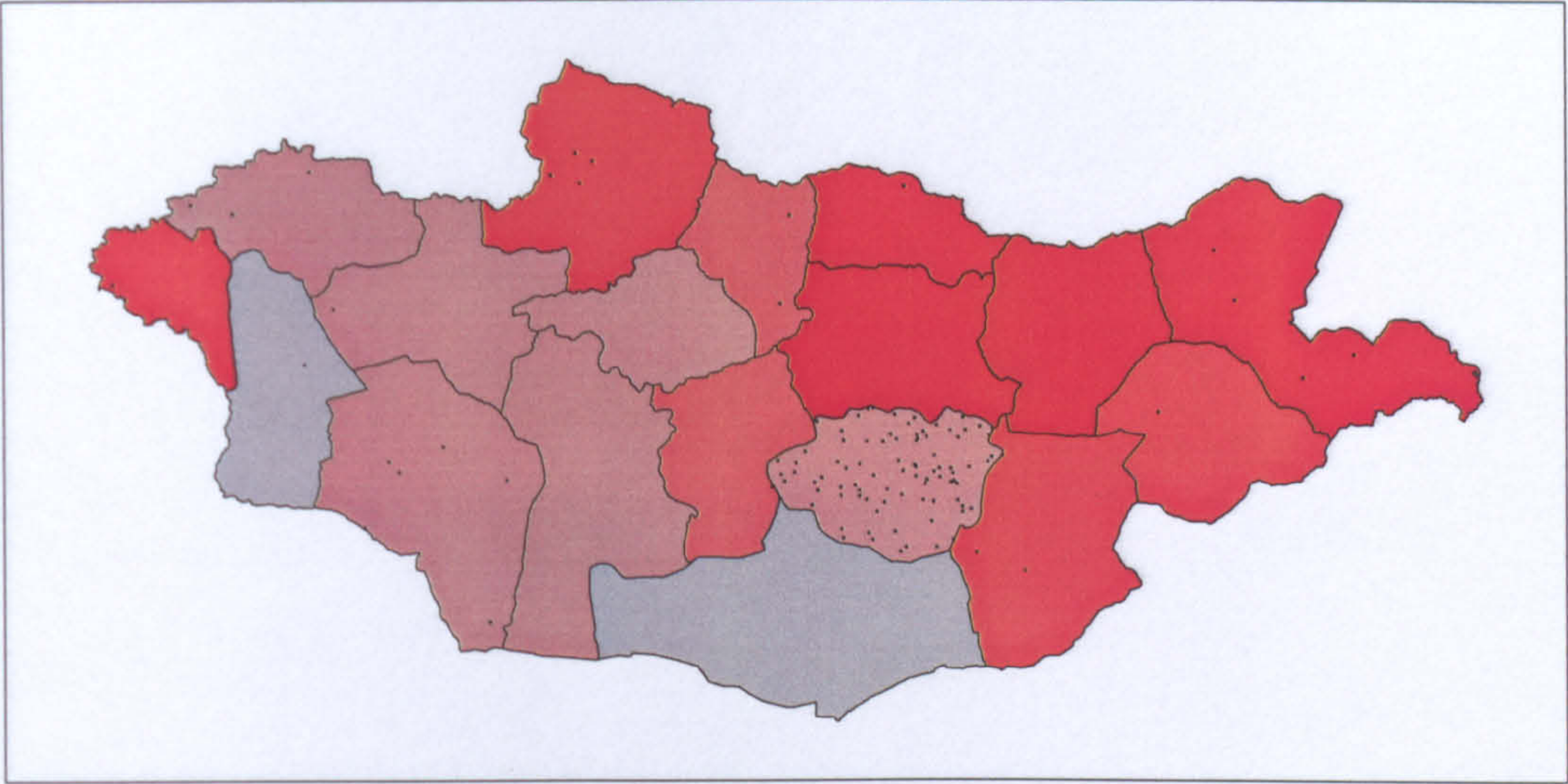
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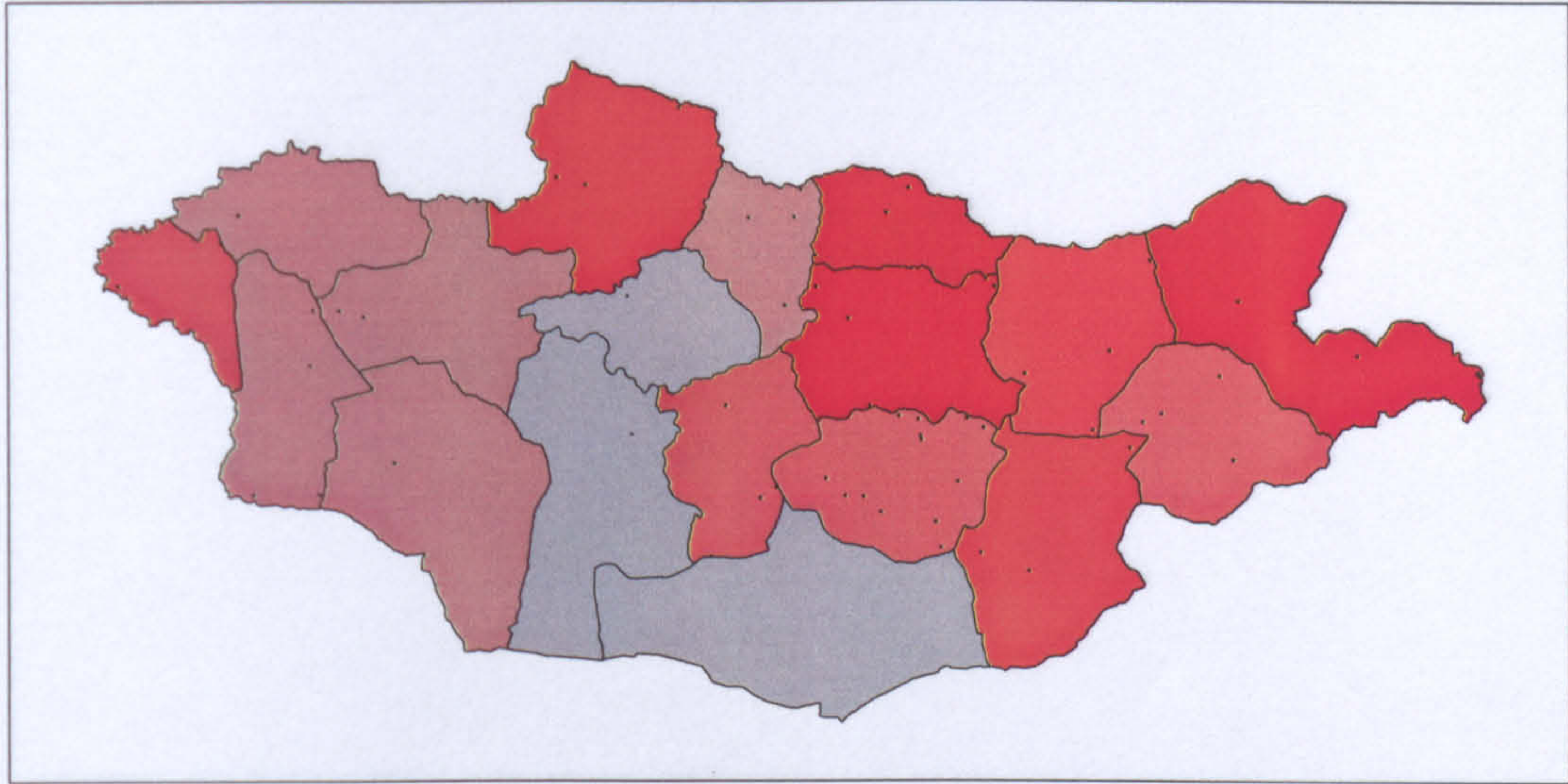
1977



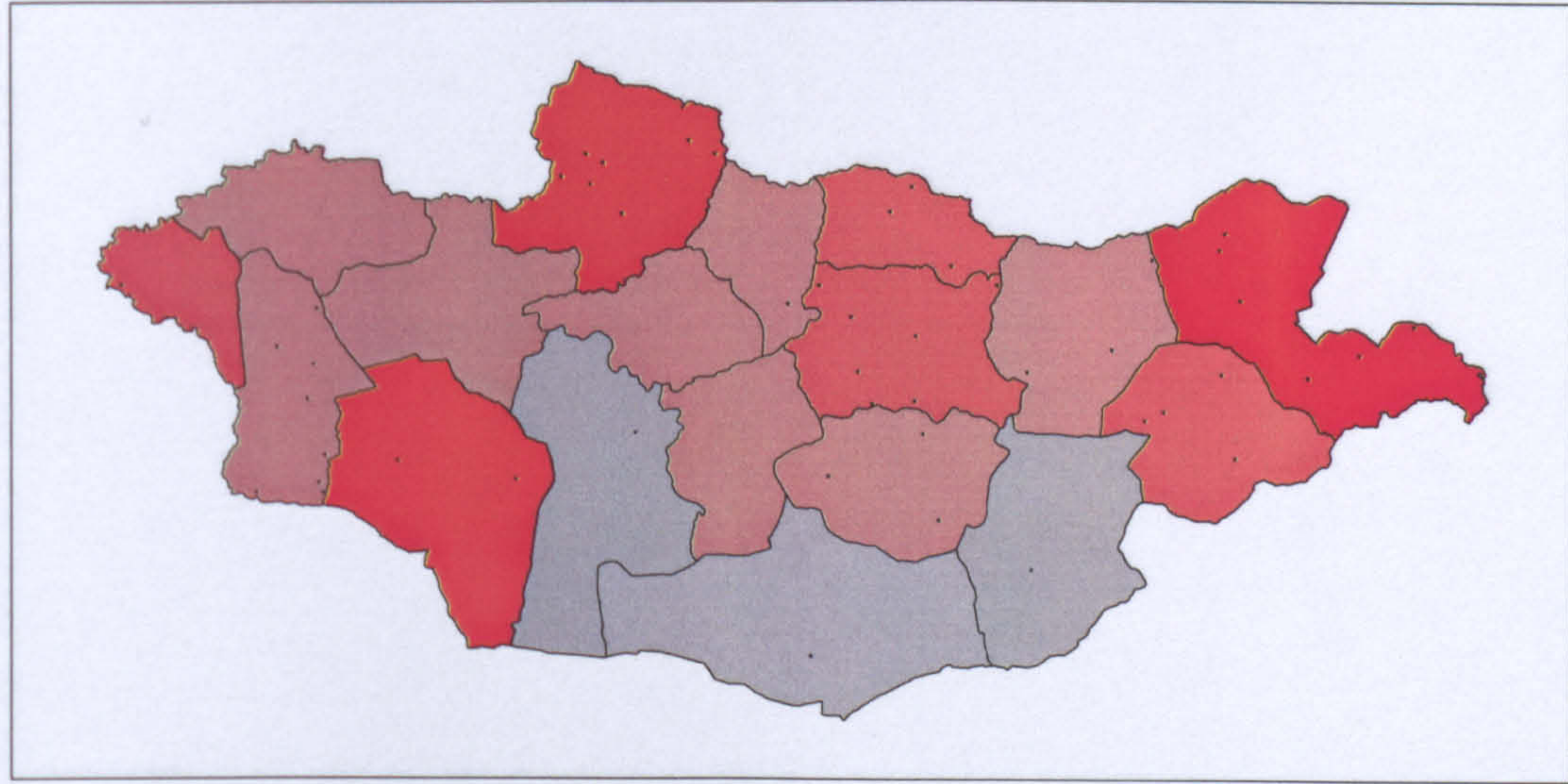
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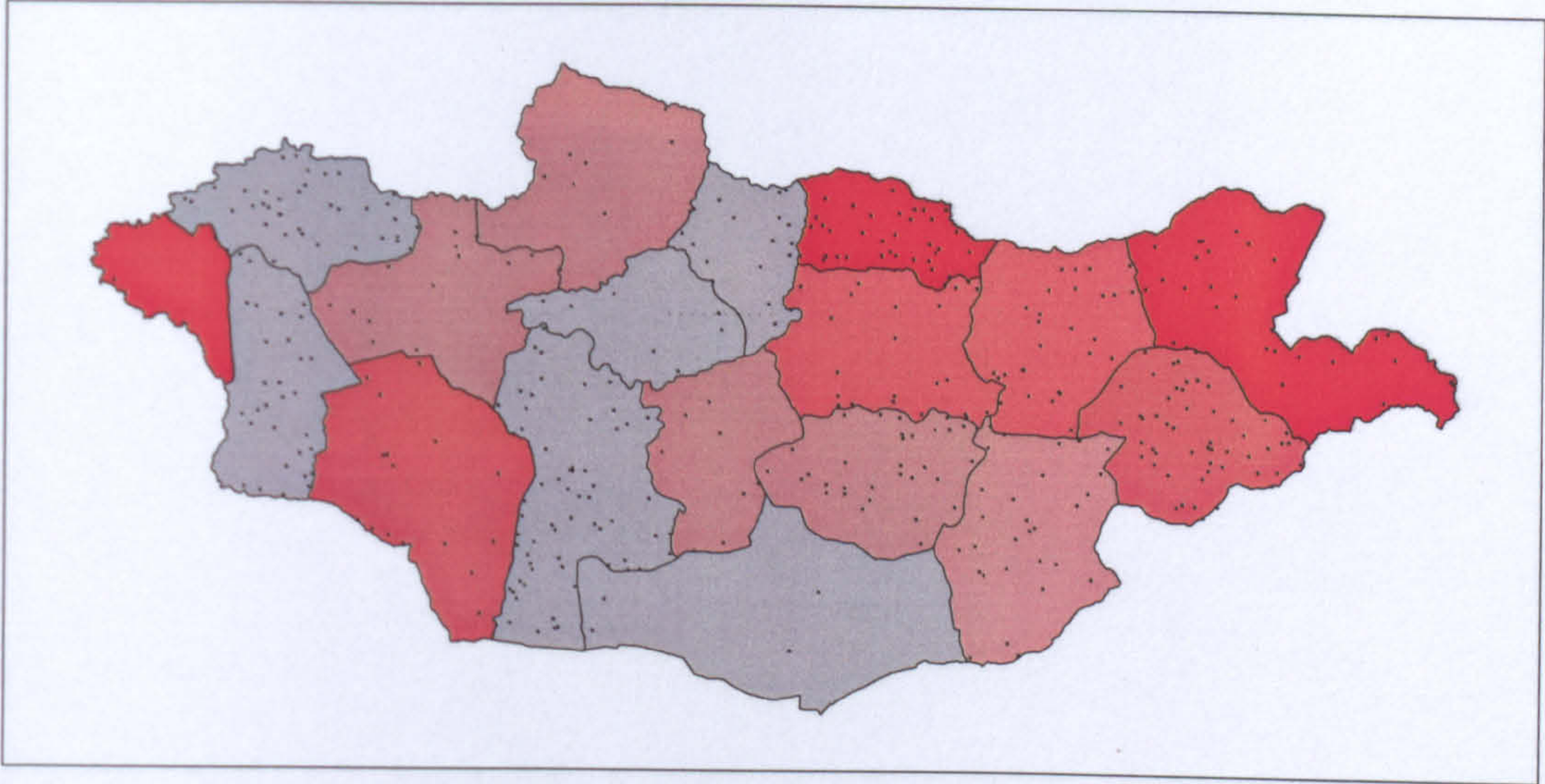
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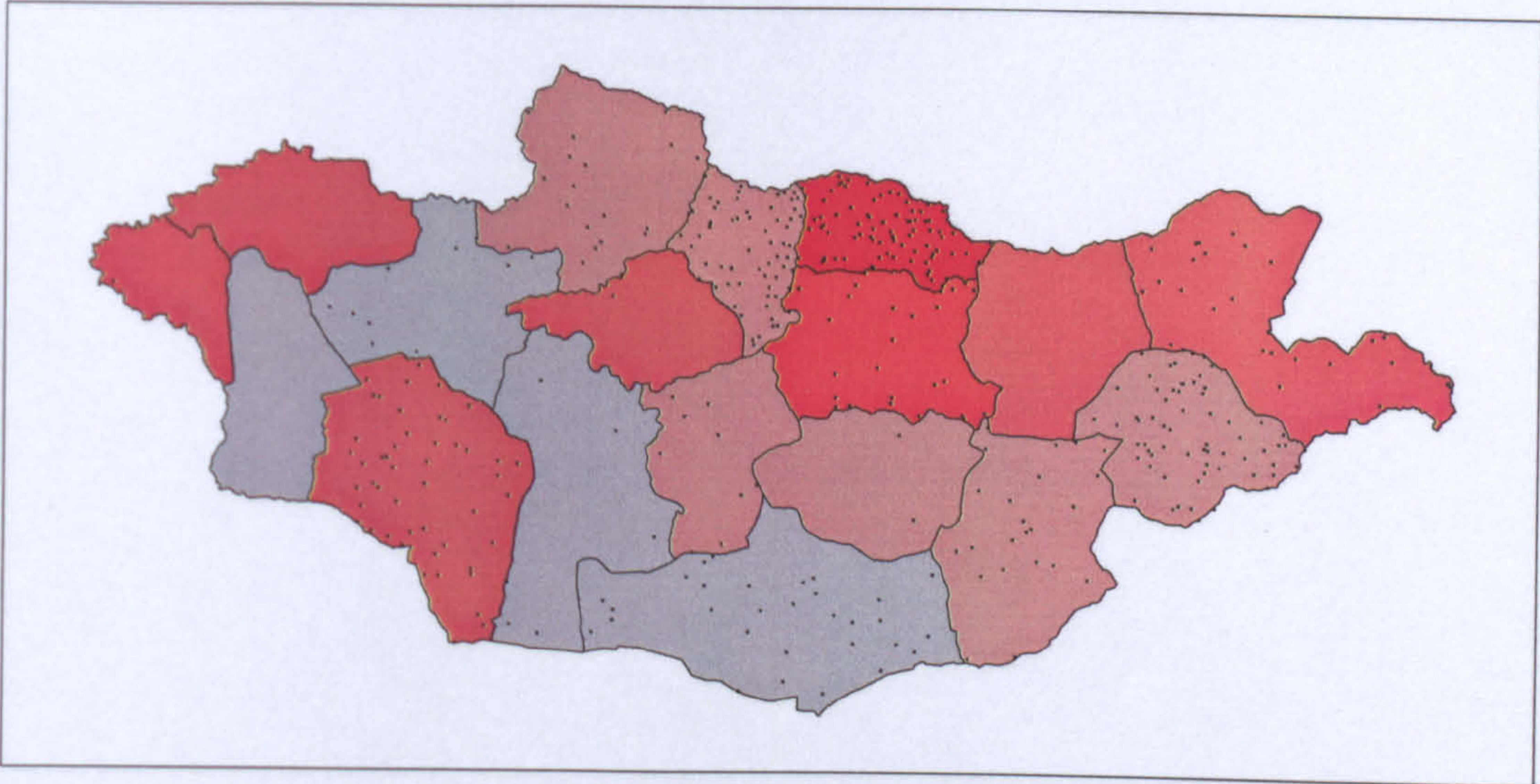
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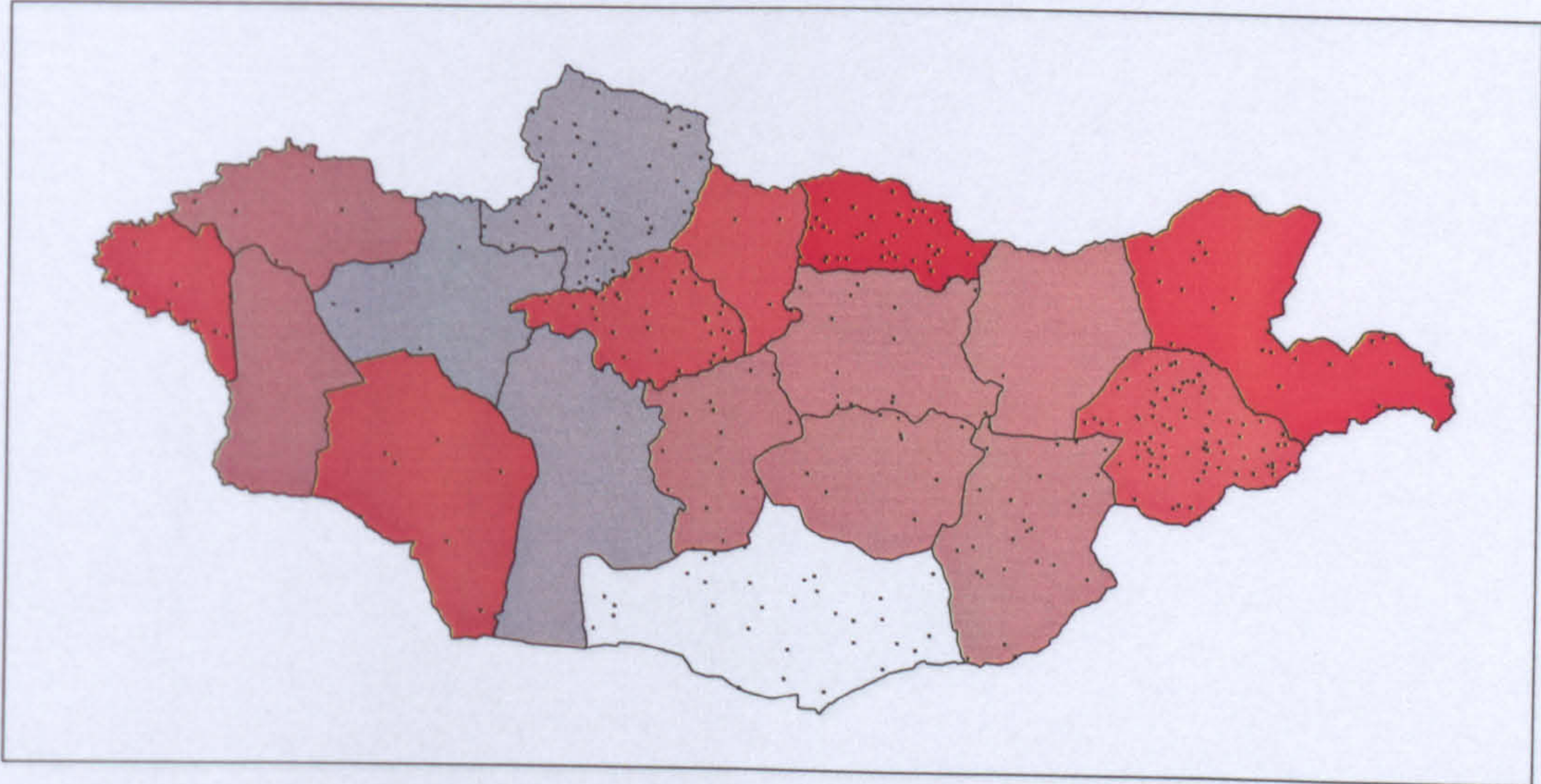
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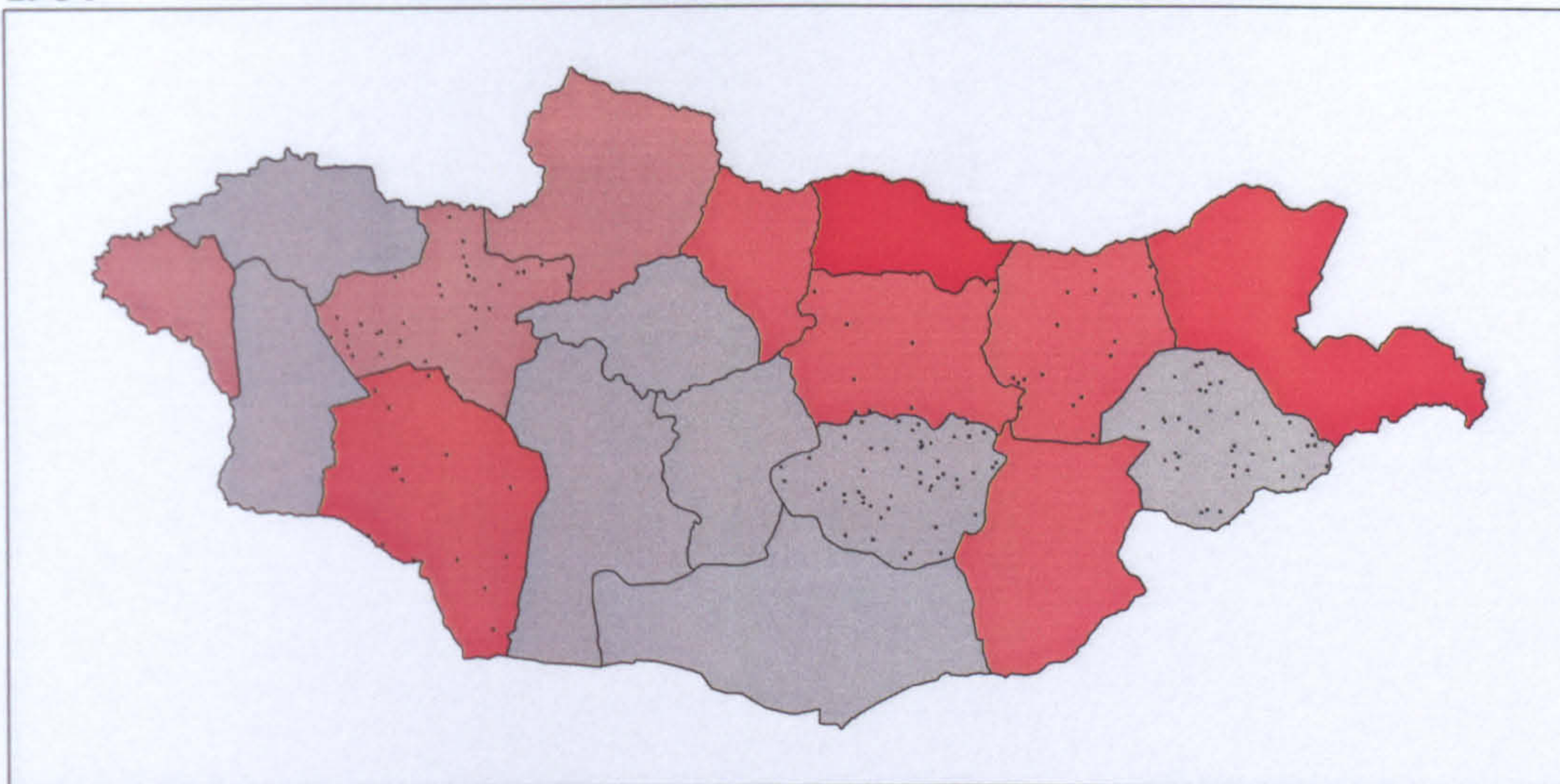
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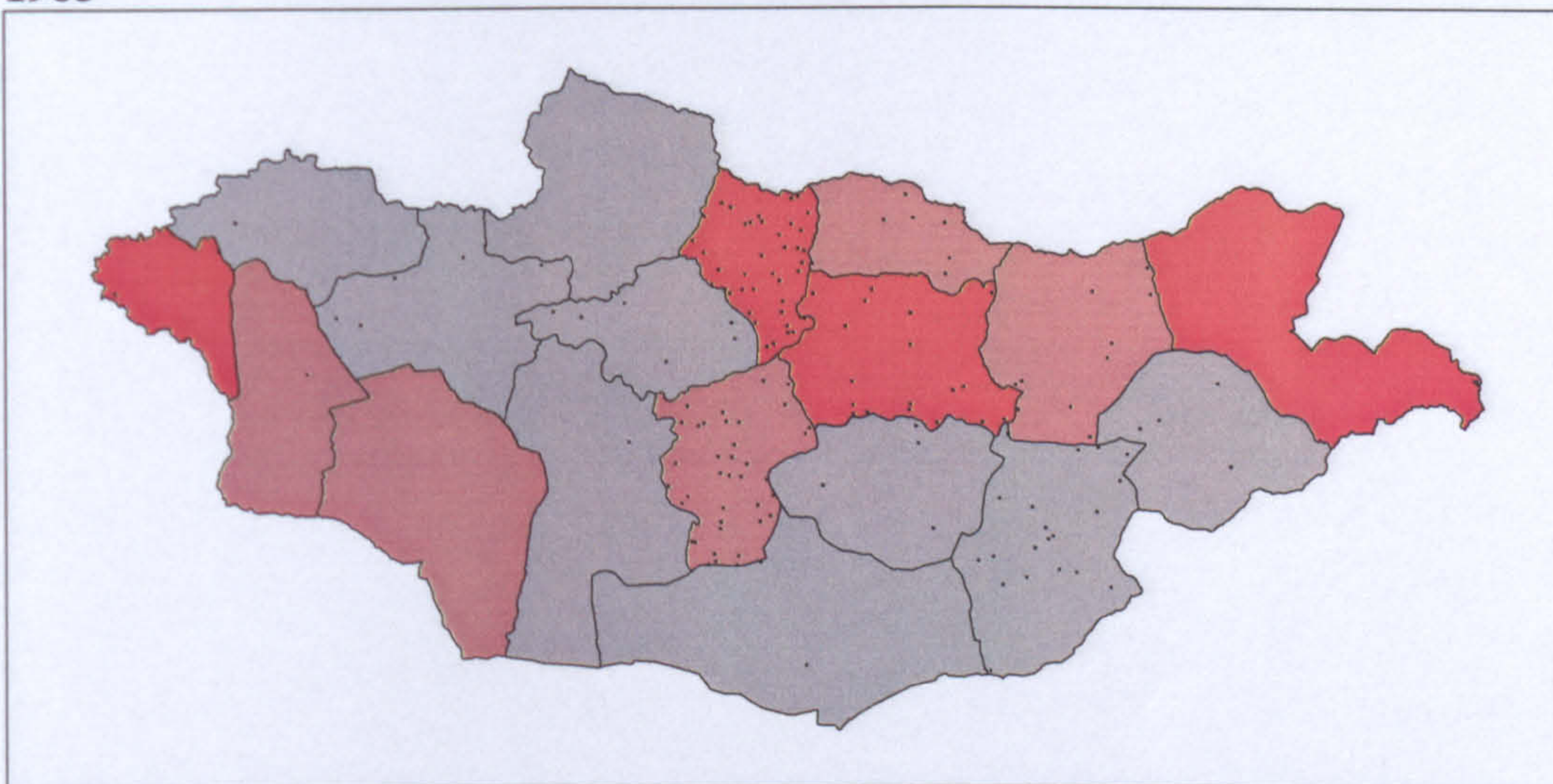
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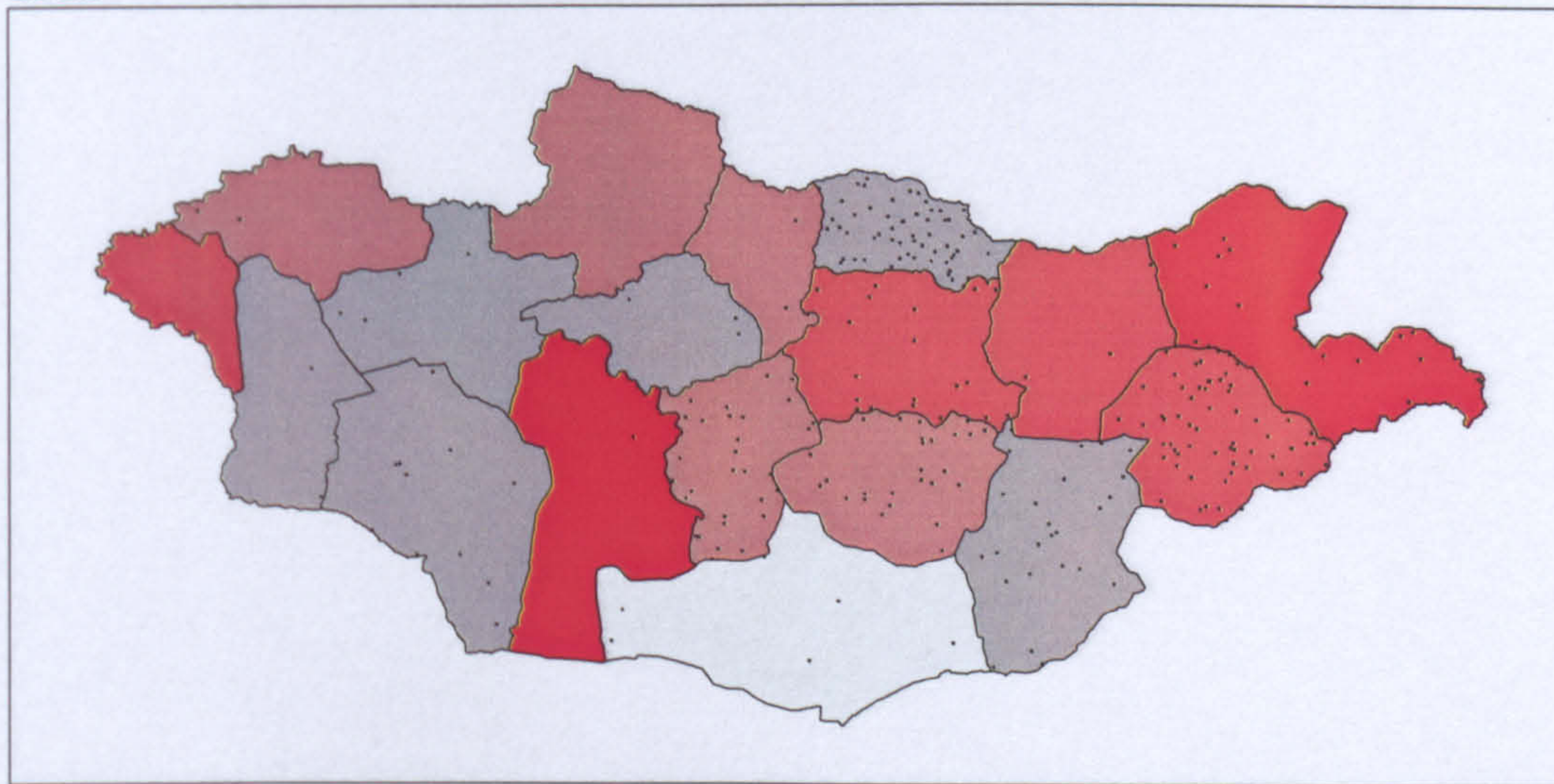
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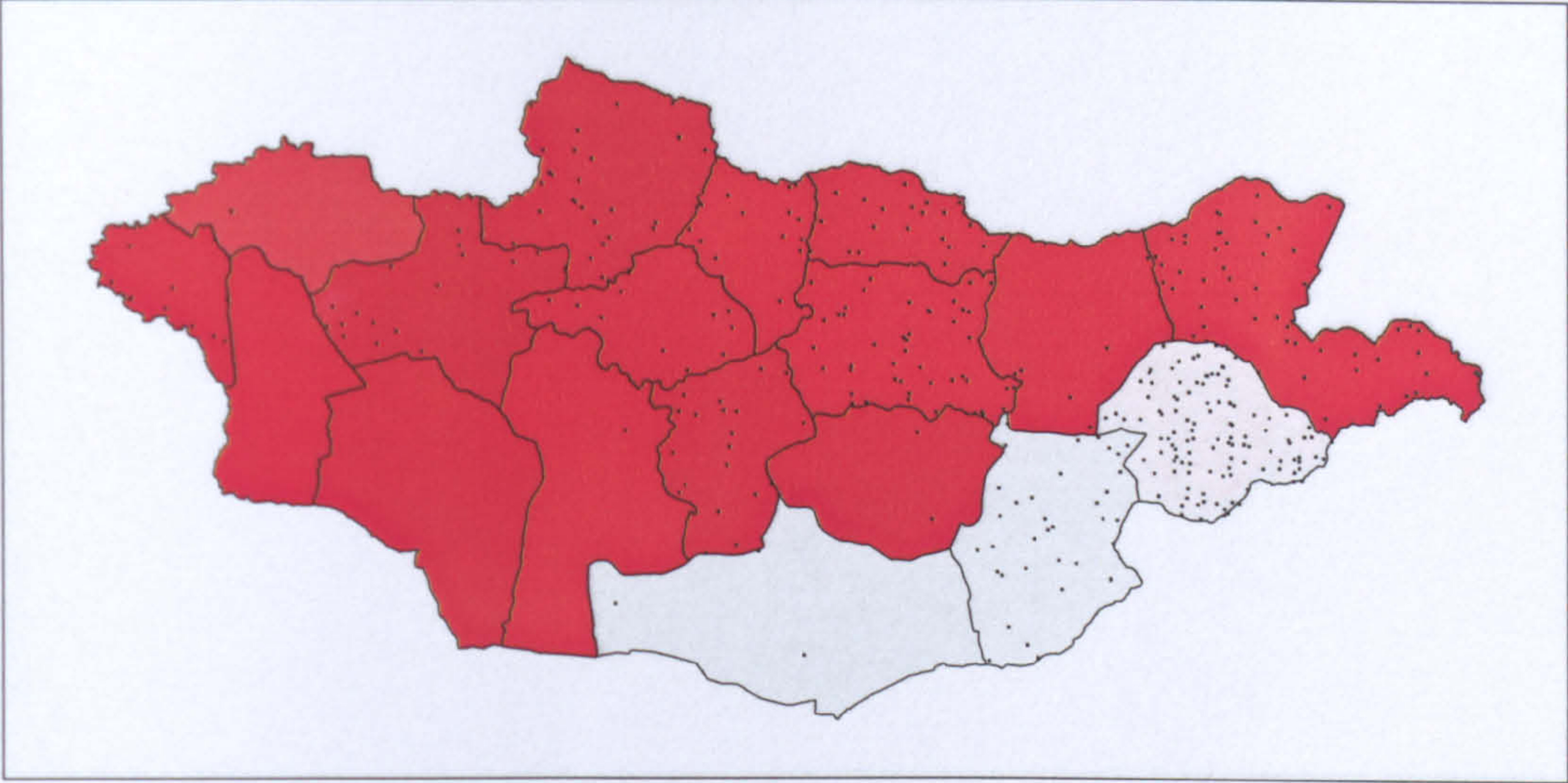
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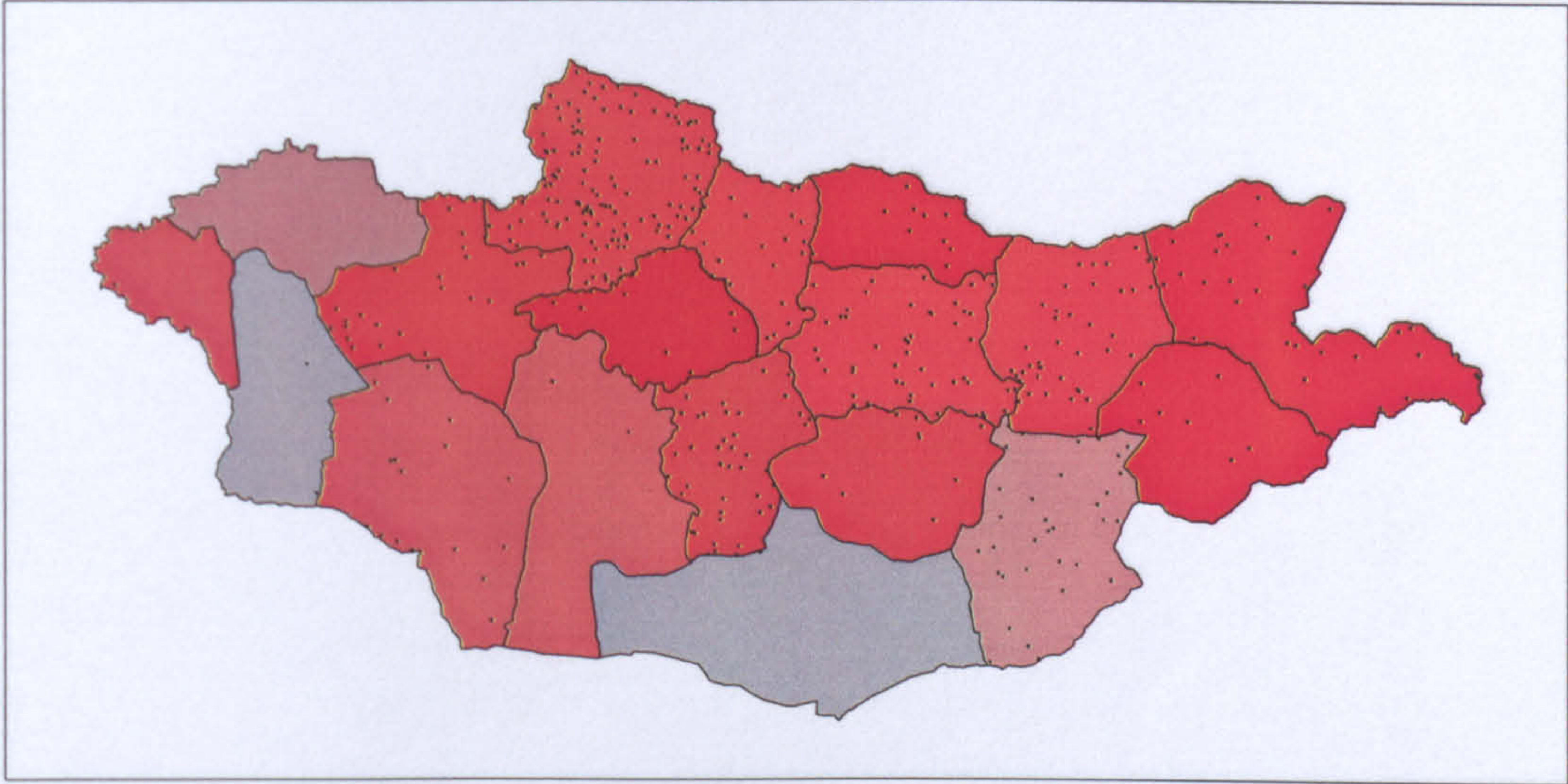
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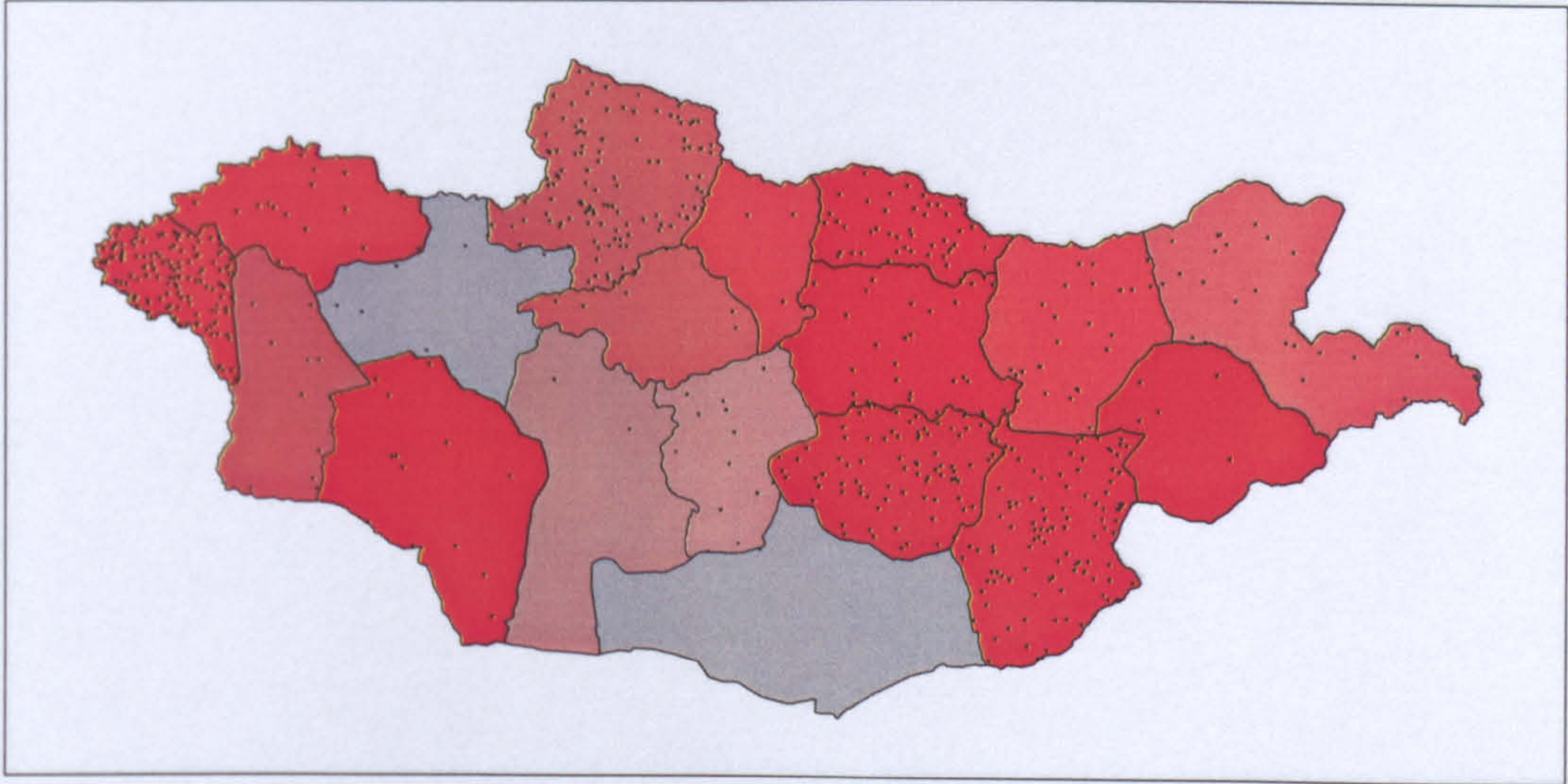
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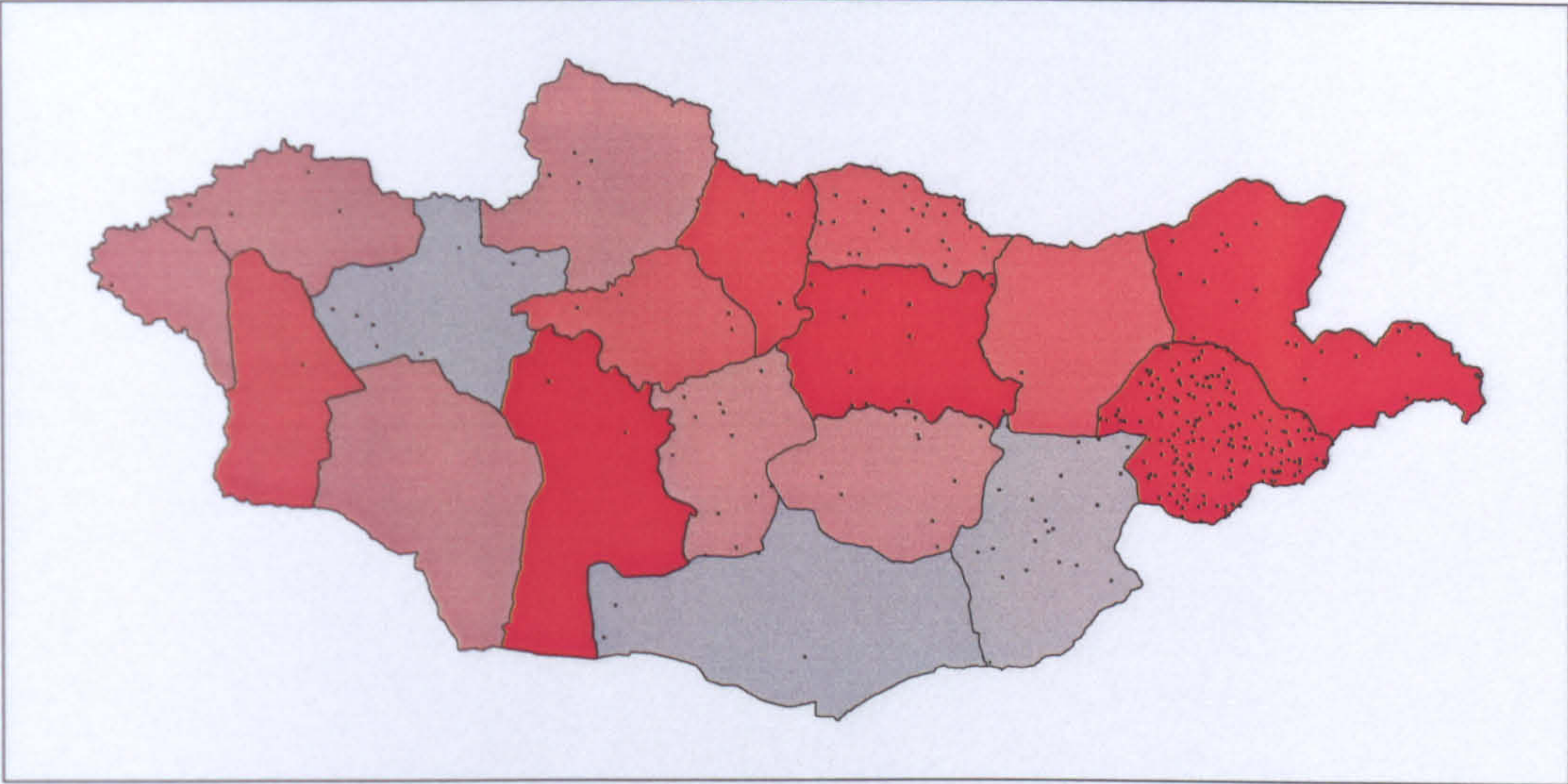
1988



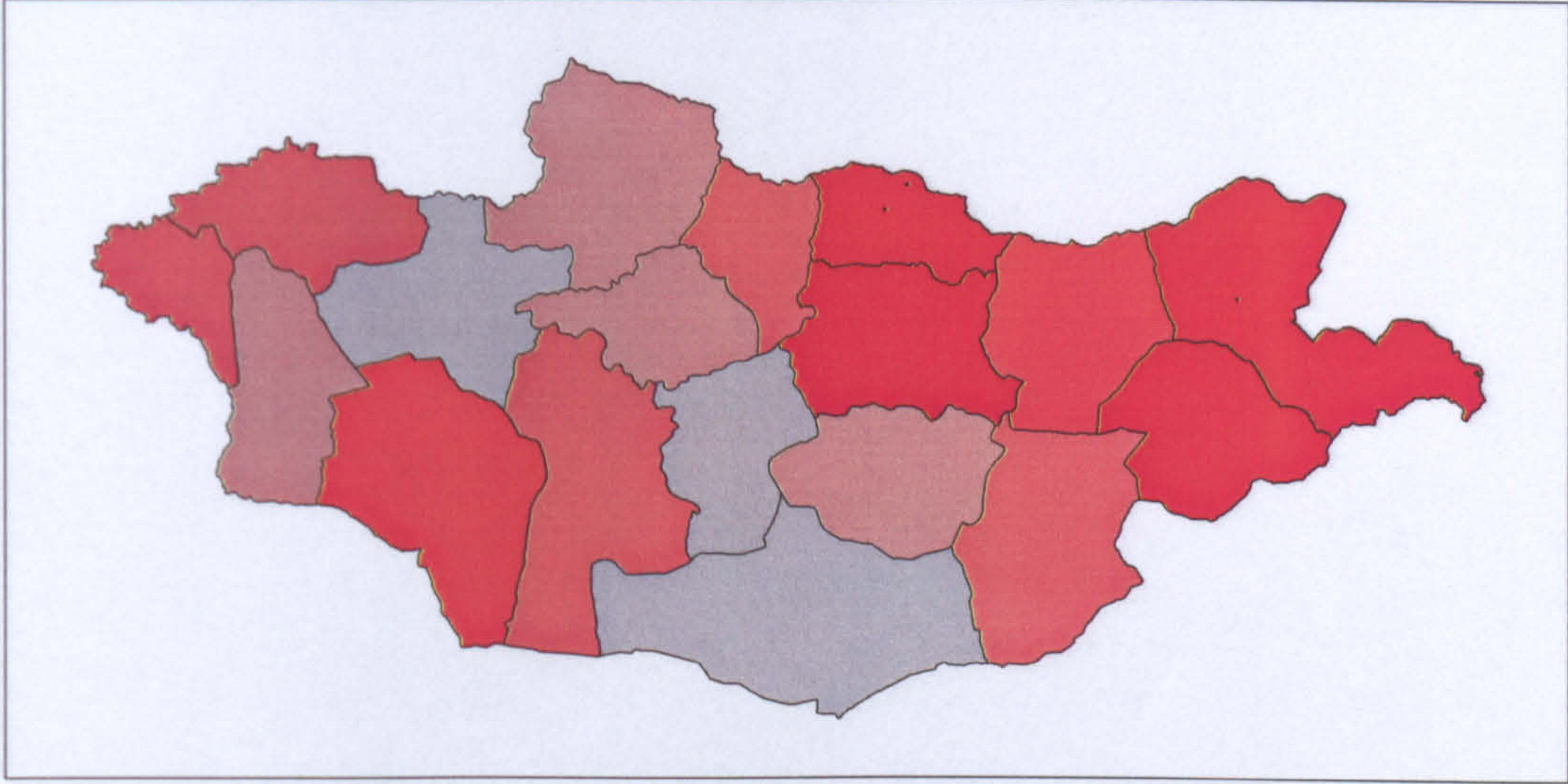
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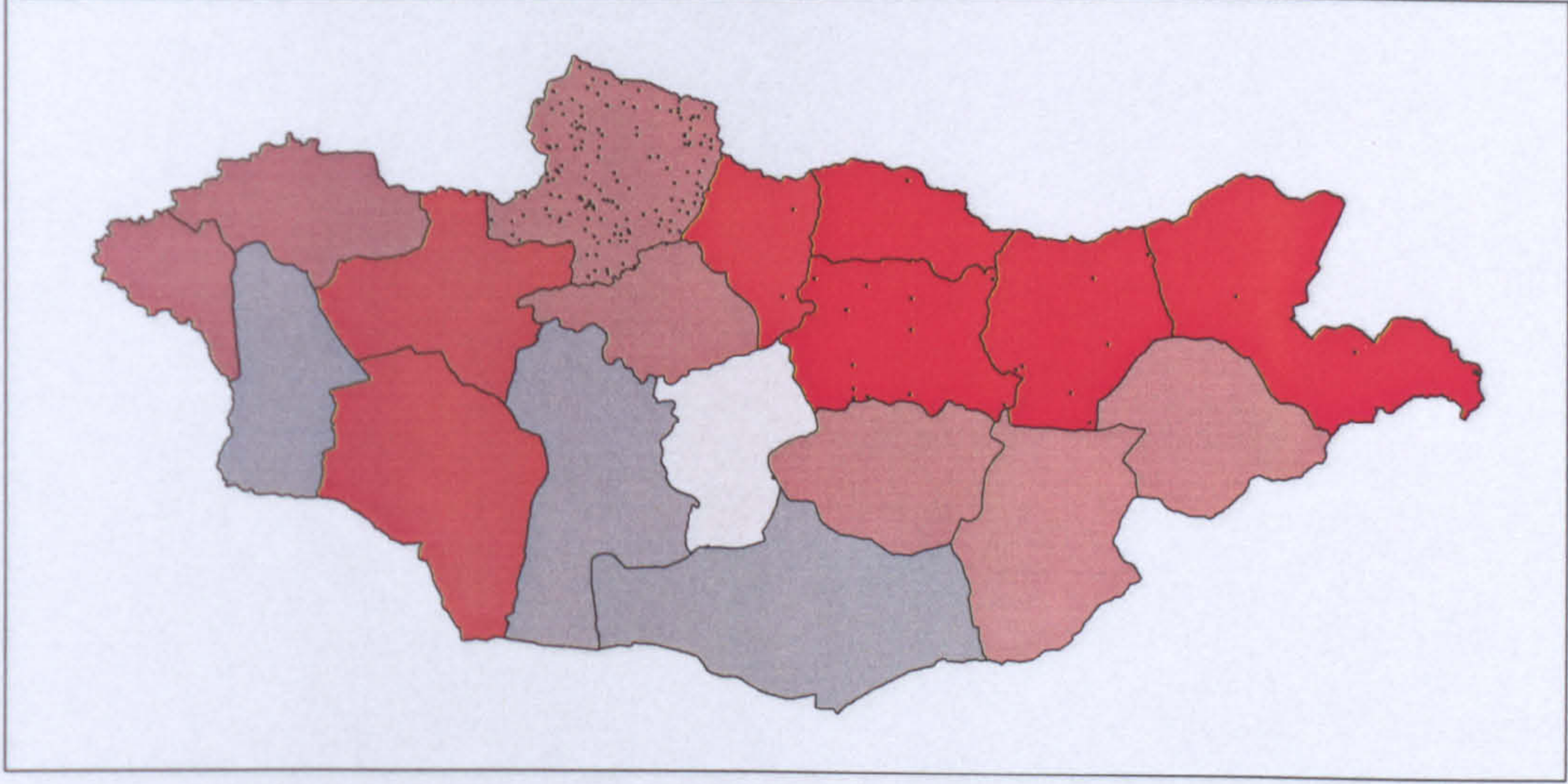
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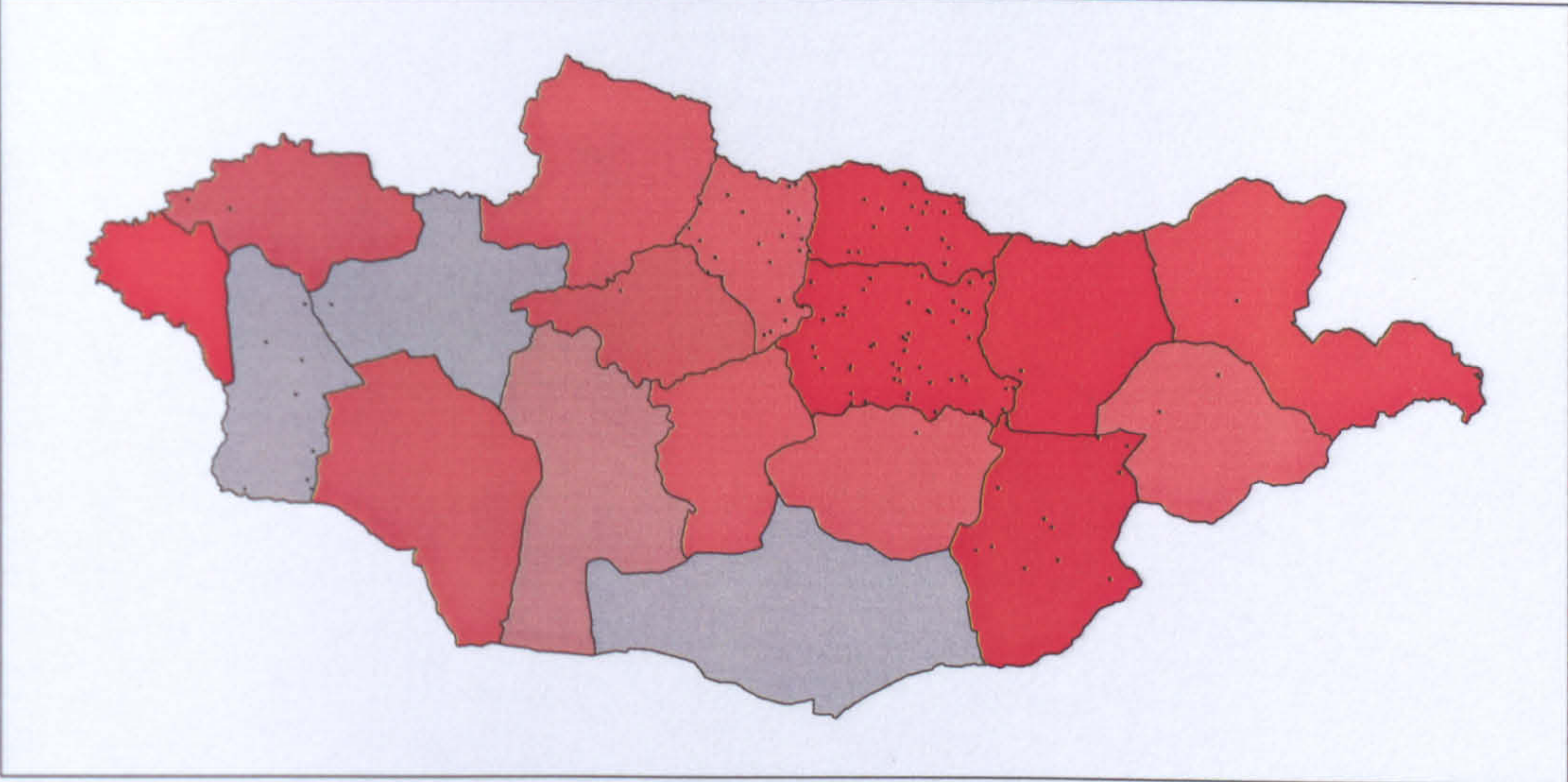
1991



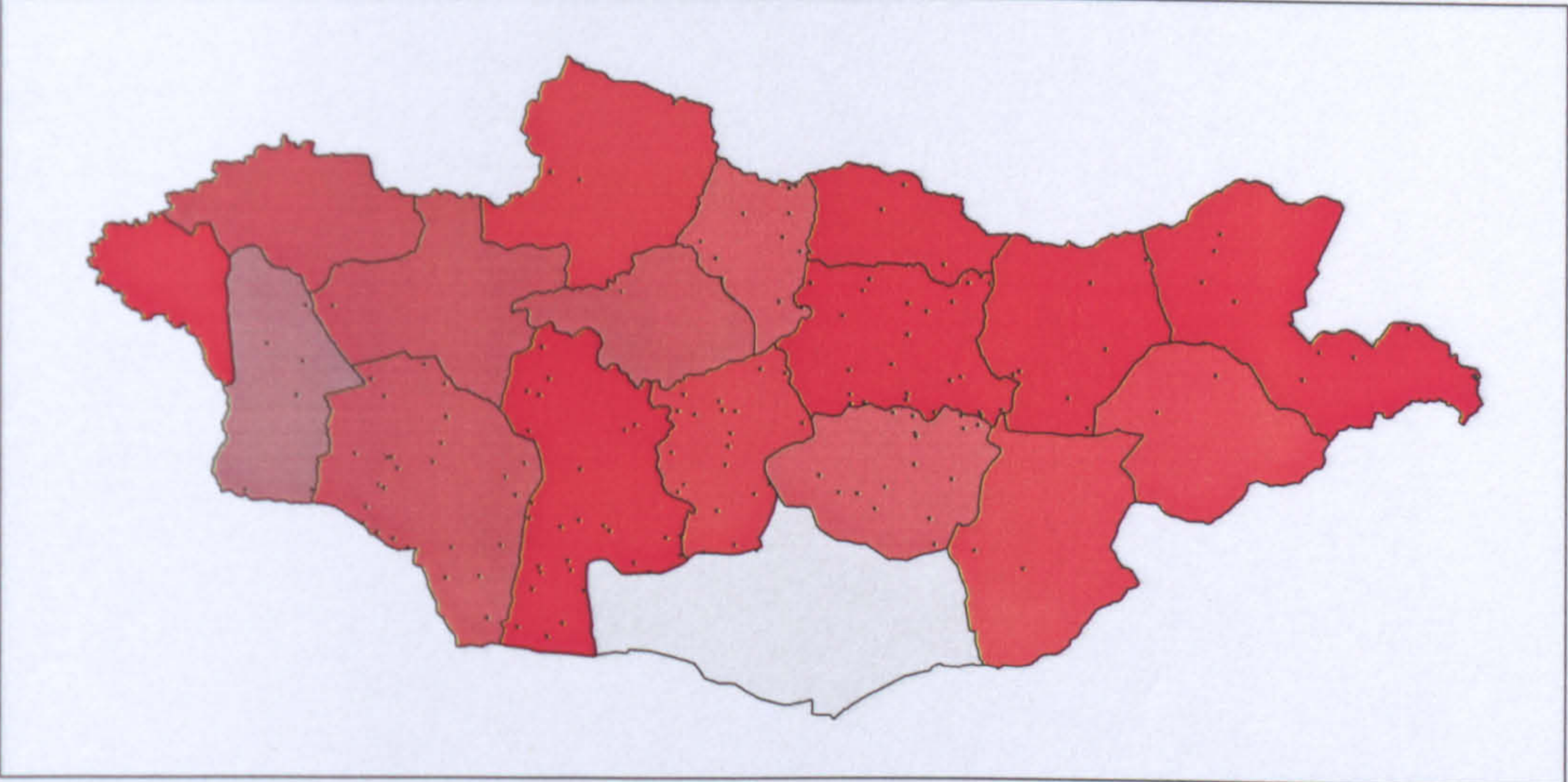
1992



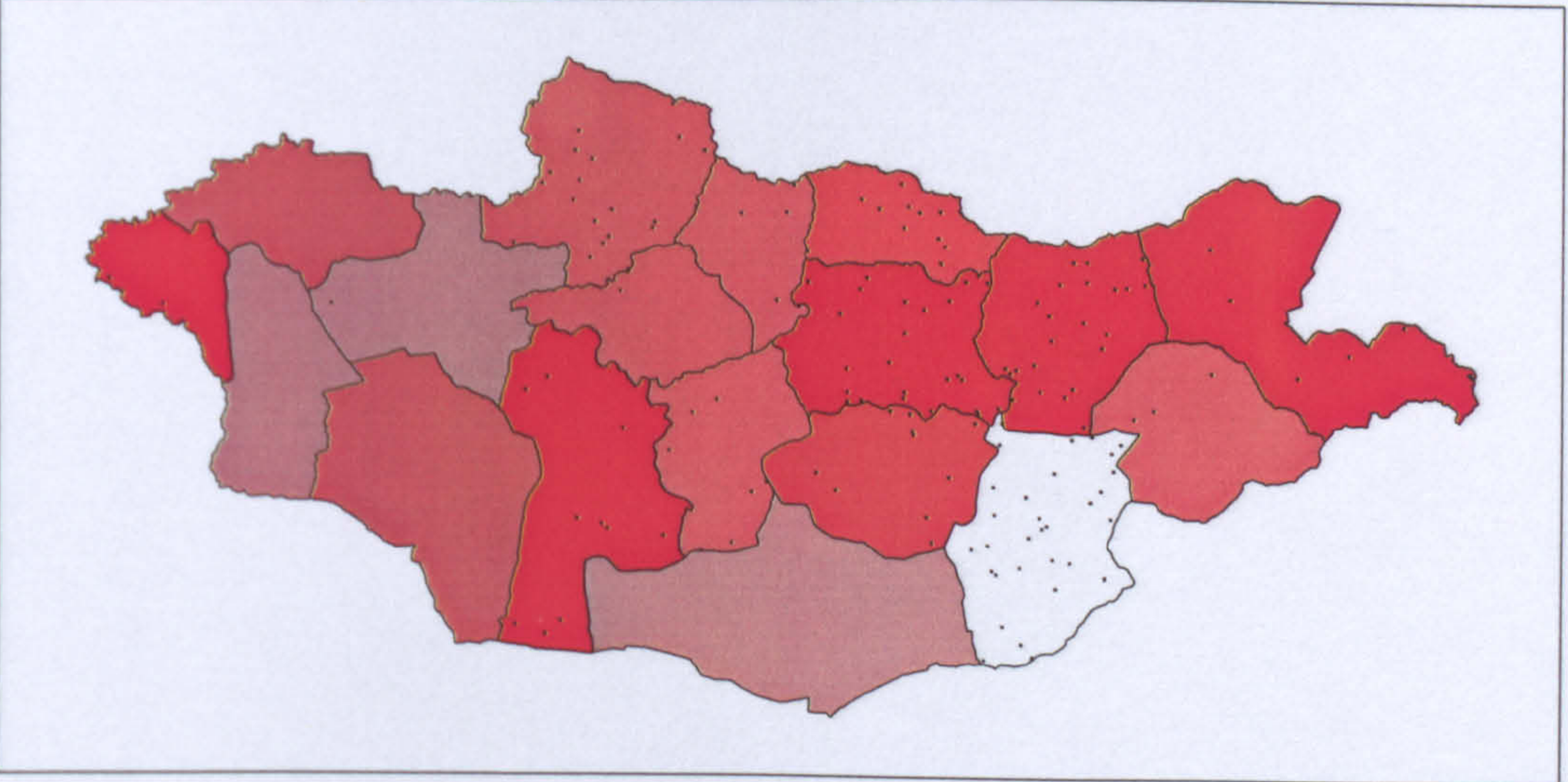
1993



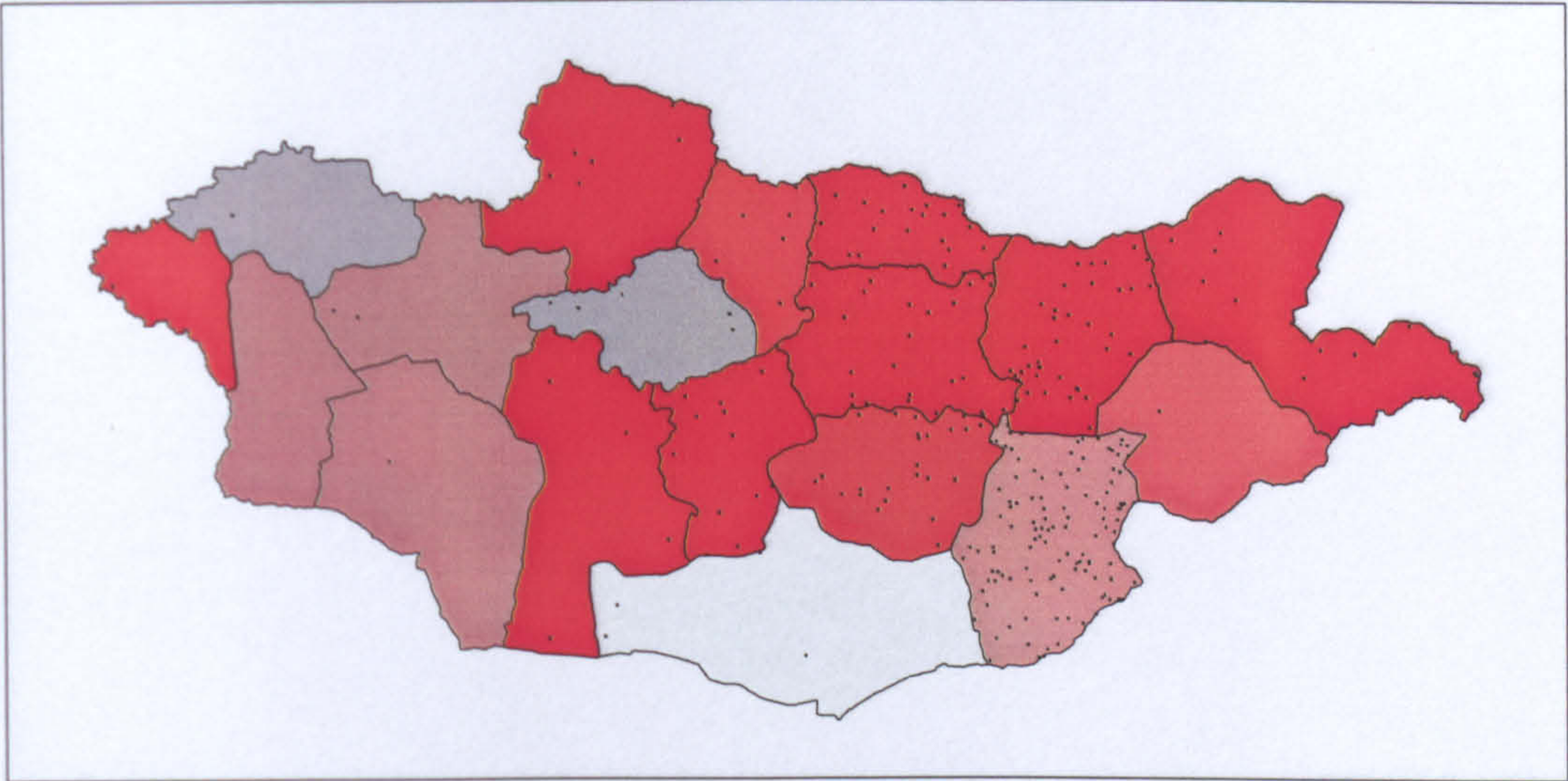
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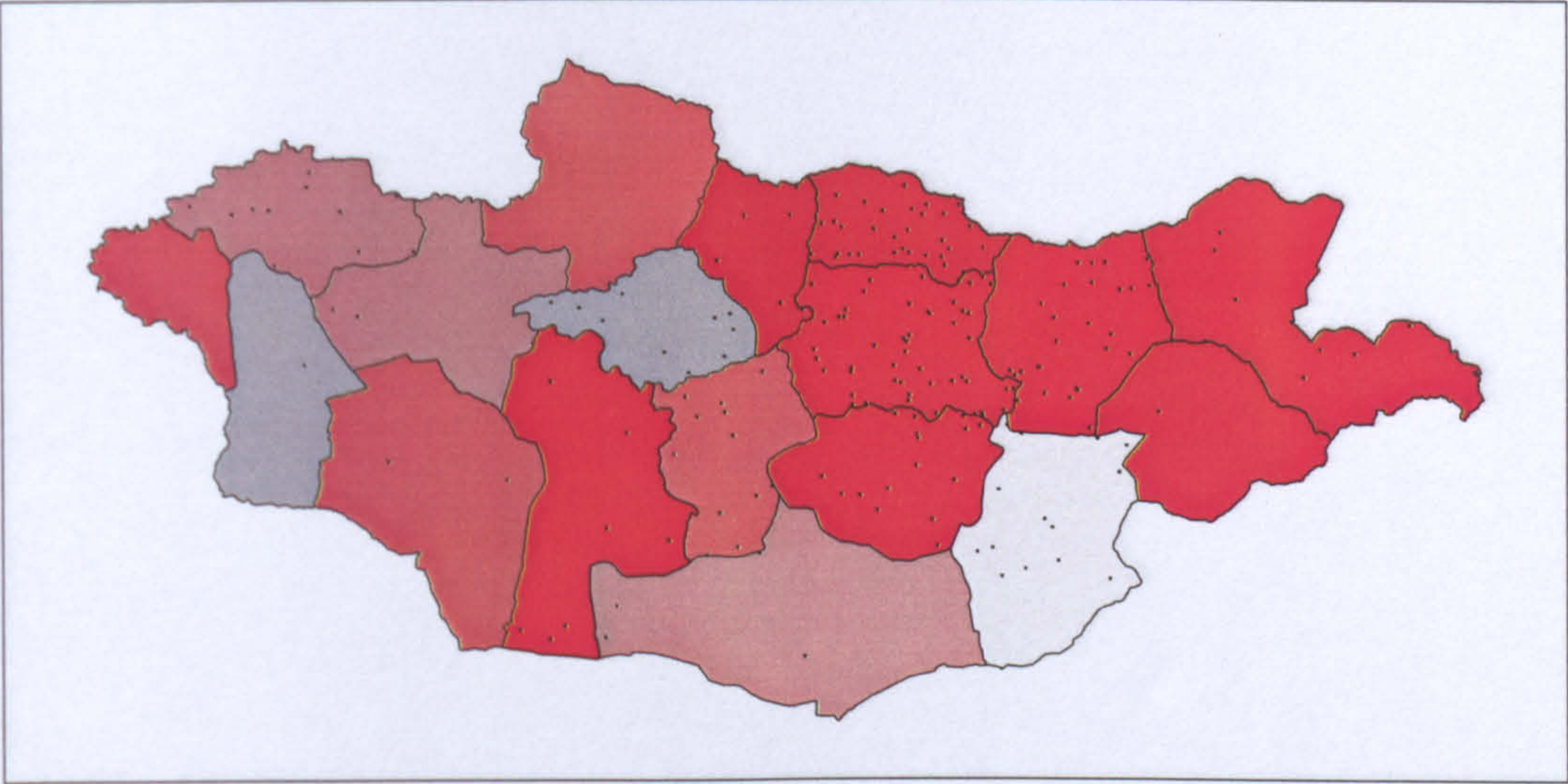
1995



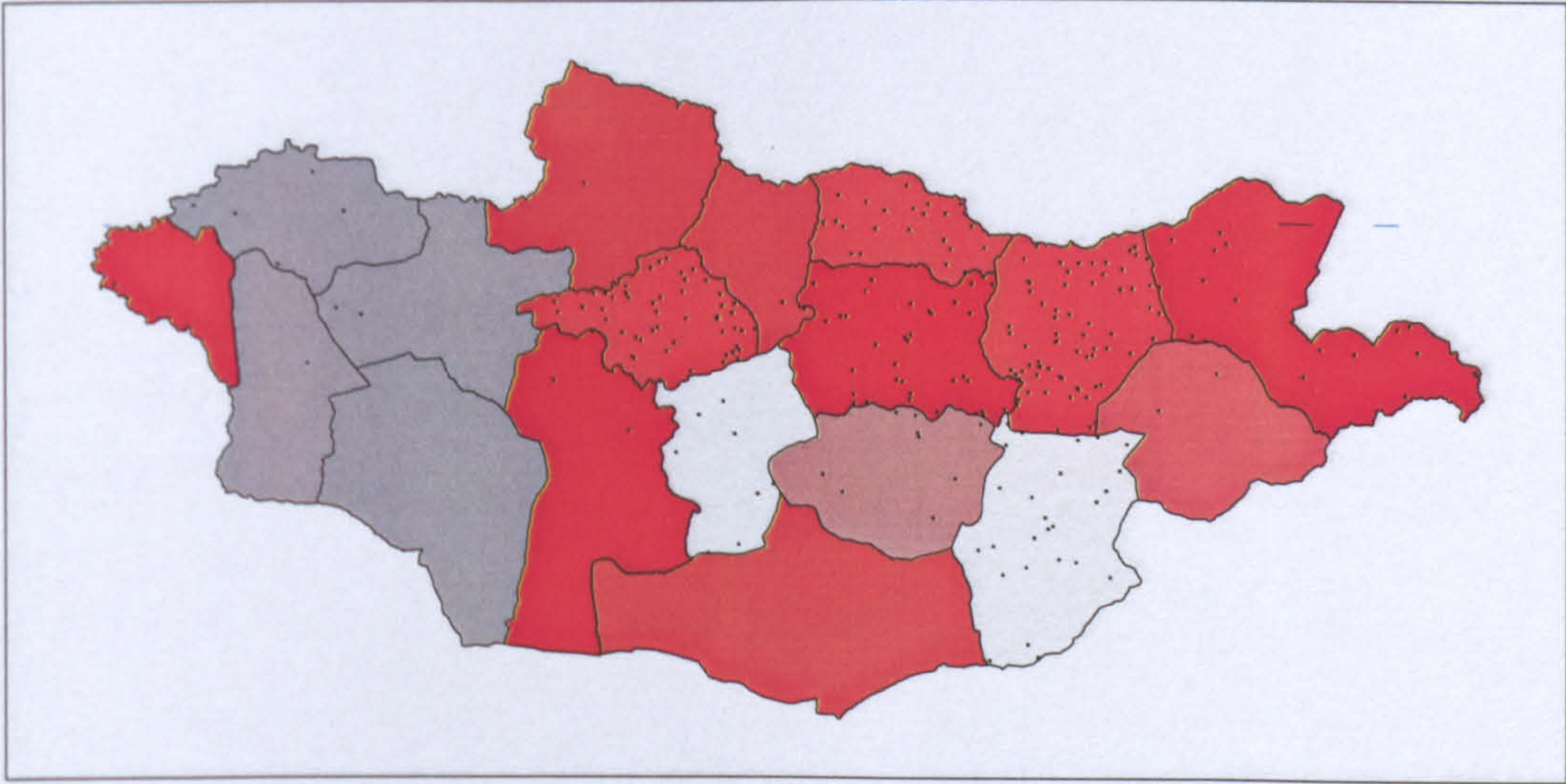
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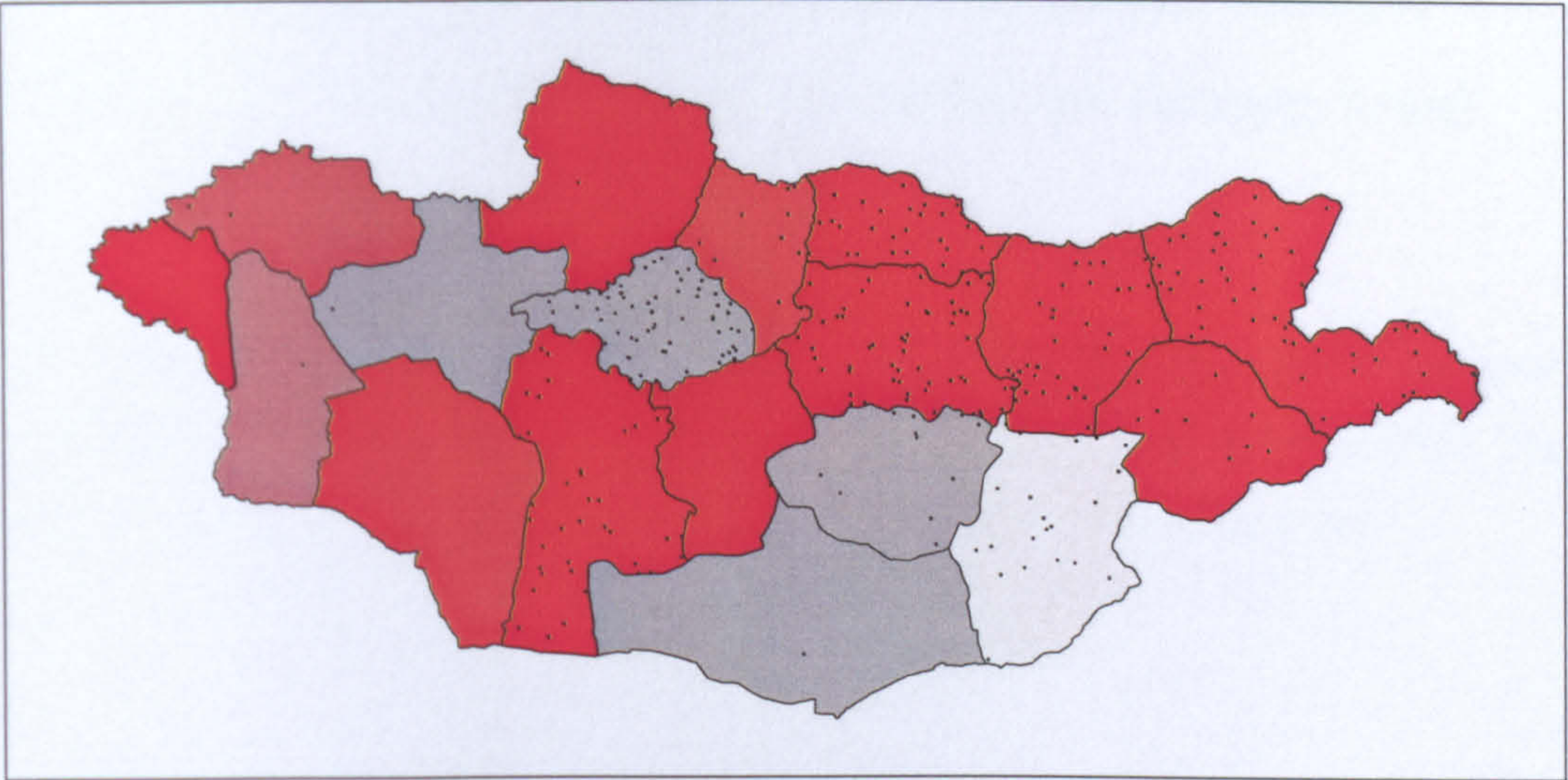
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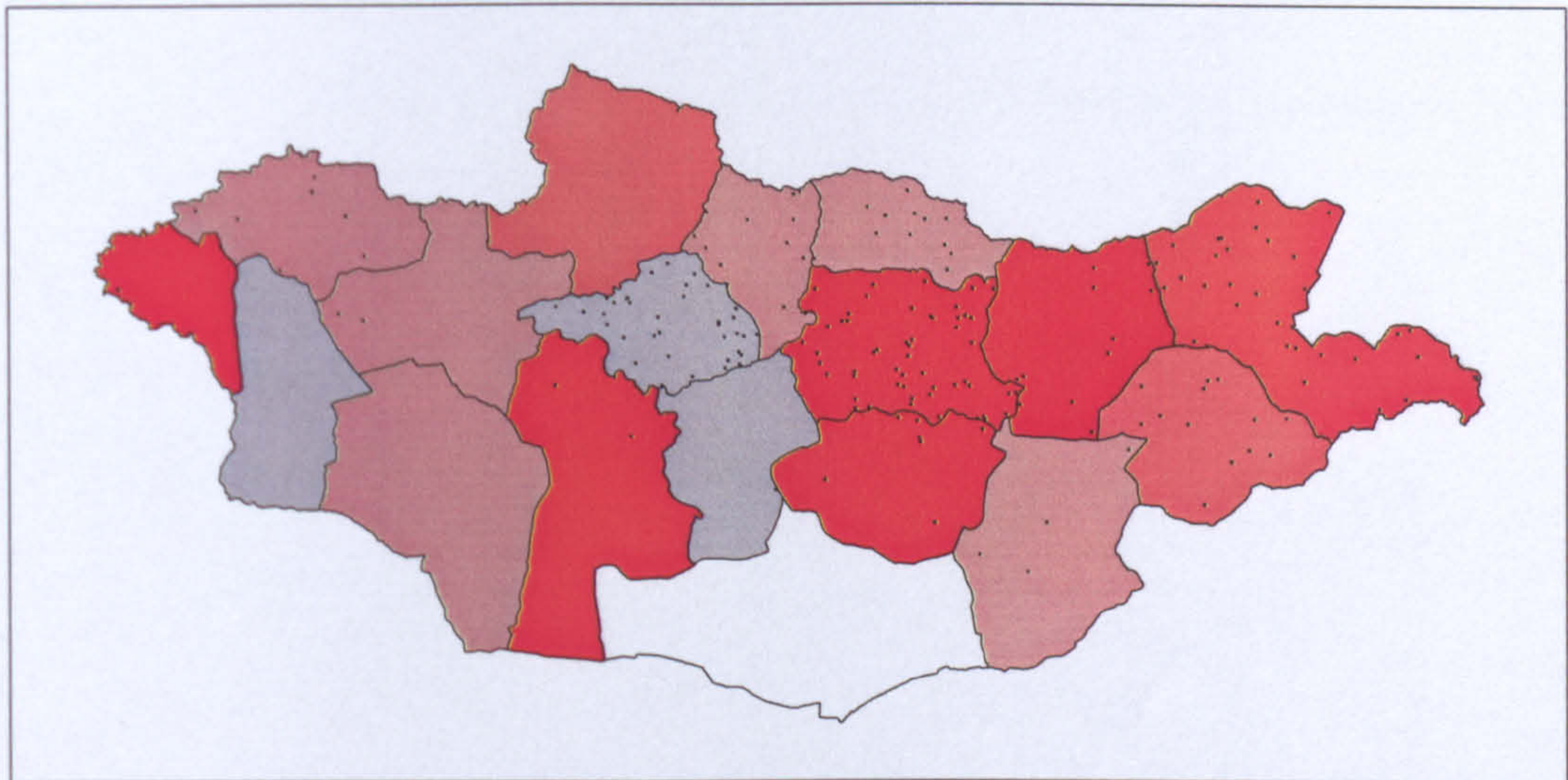
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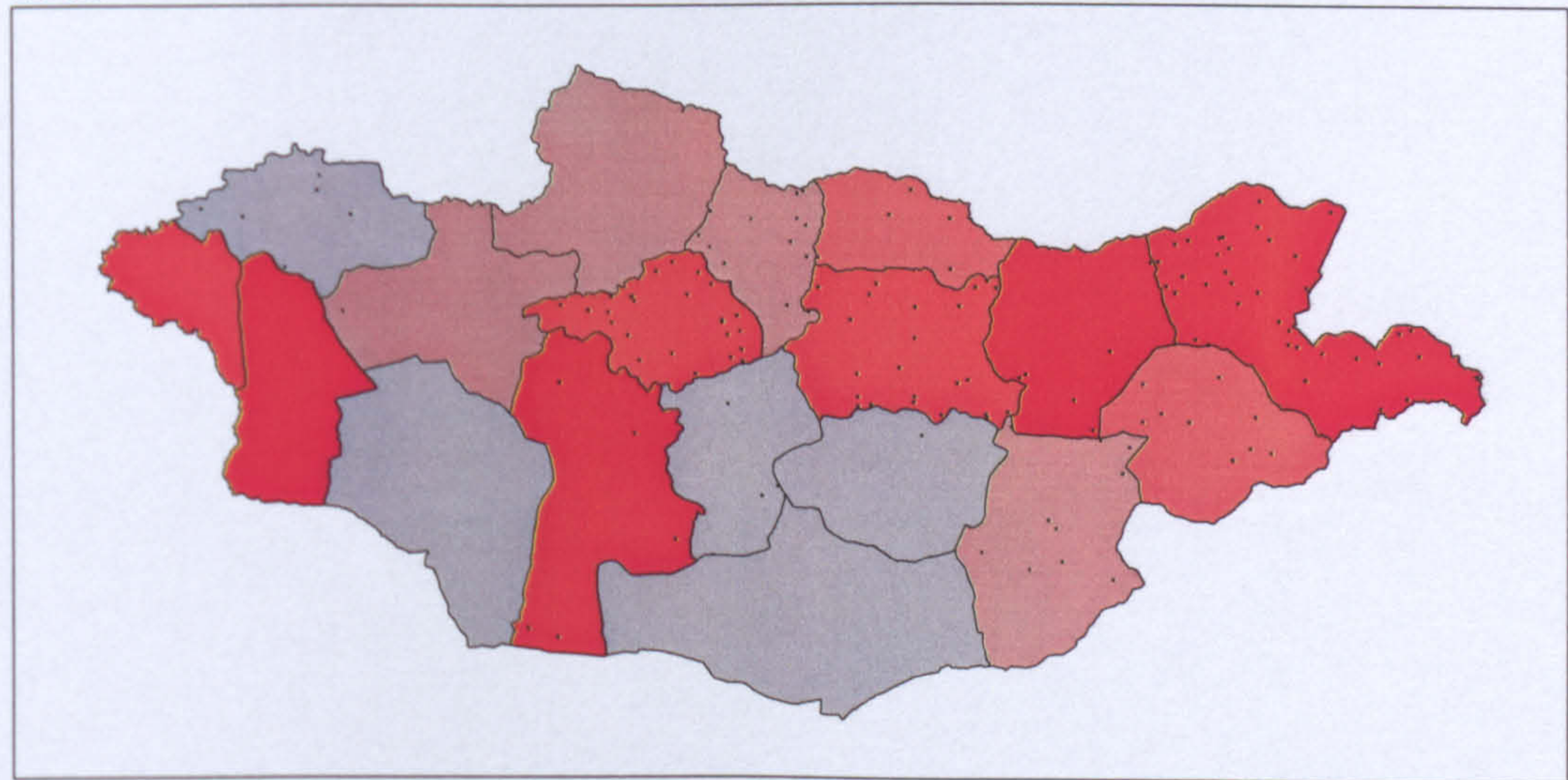
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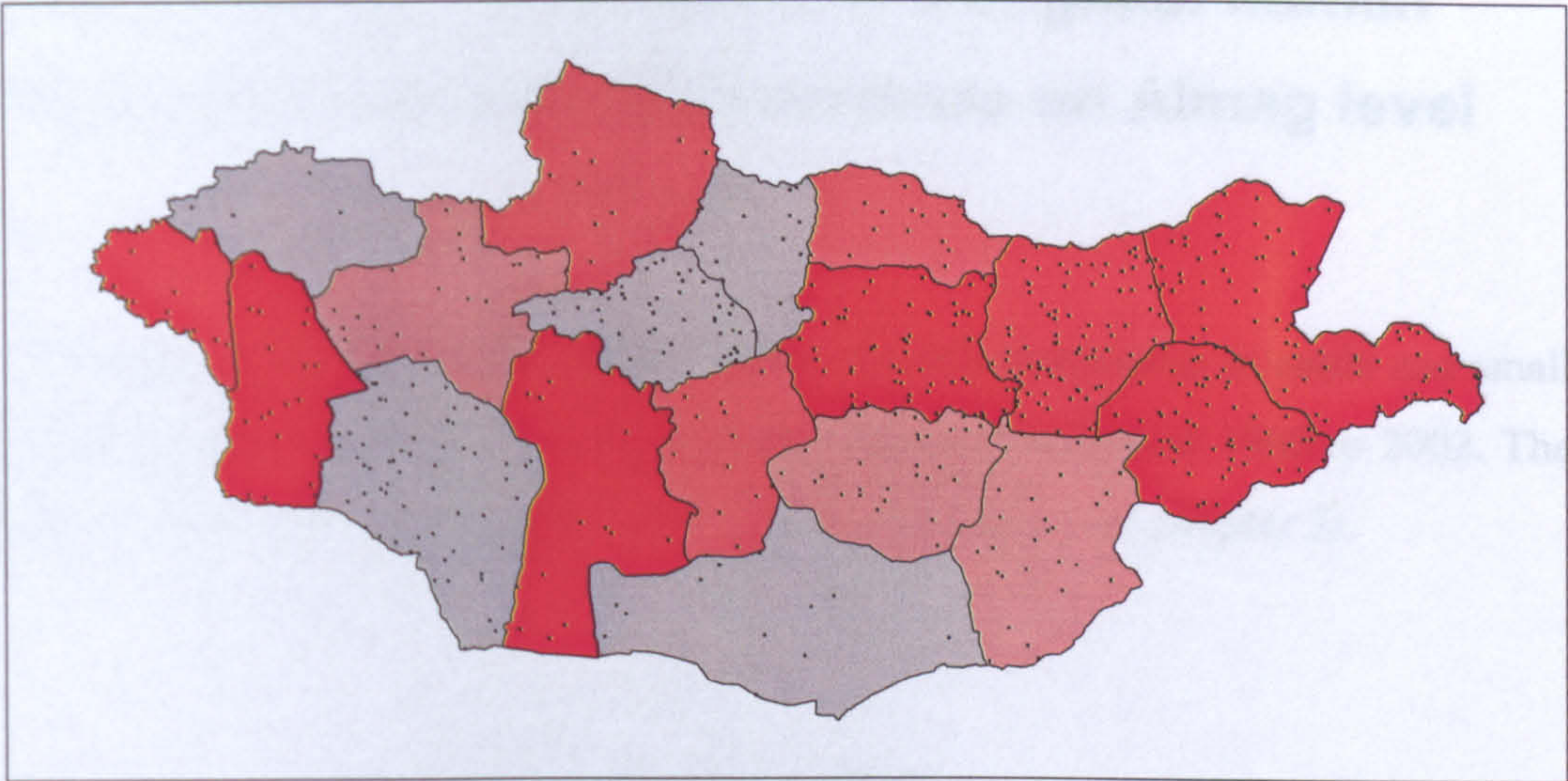
2000



2001

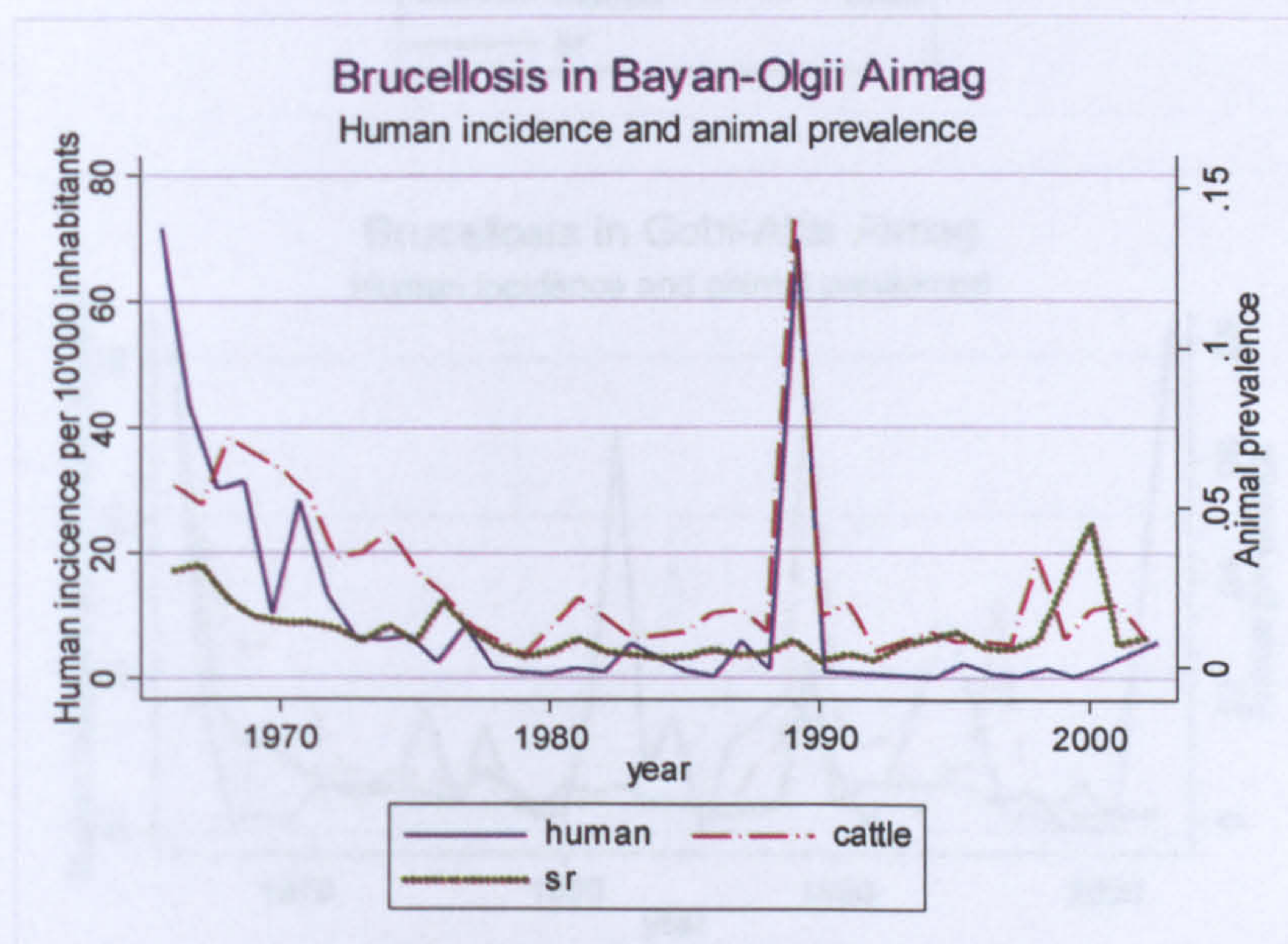
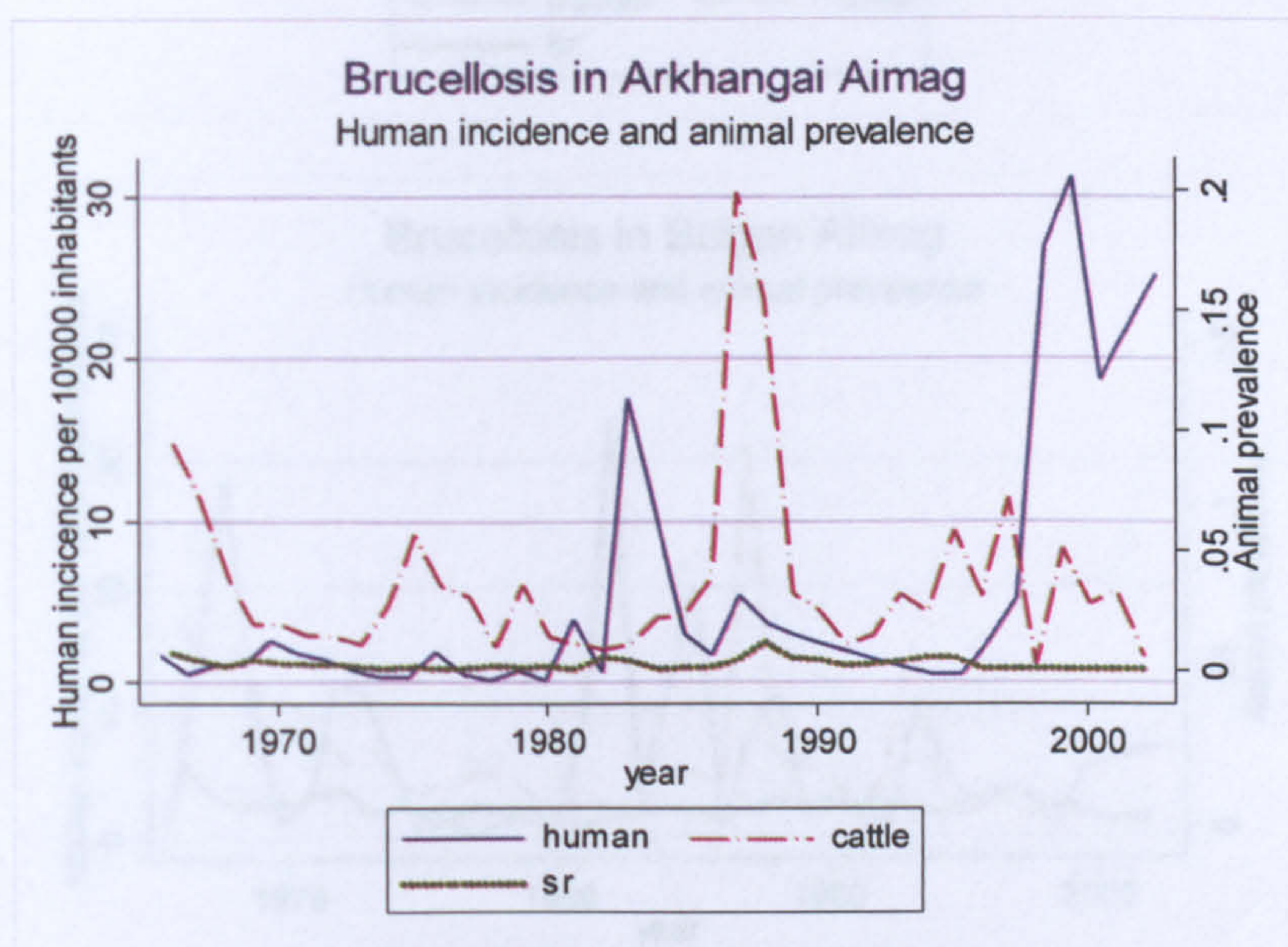


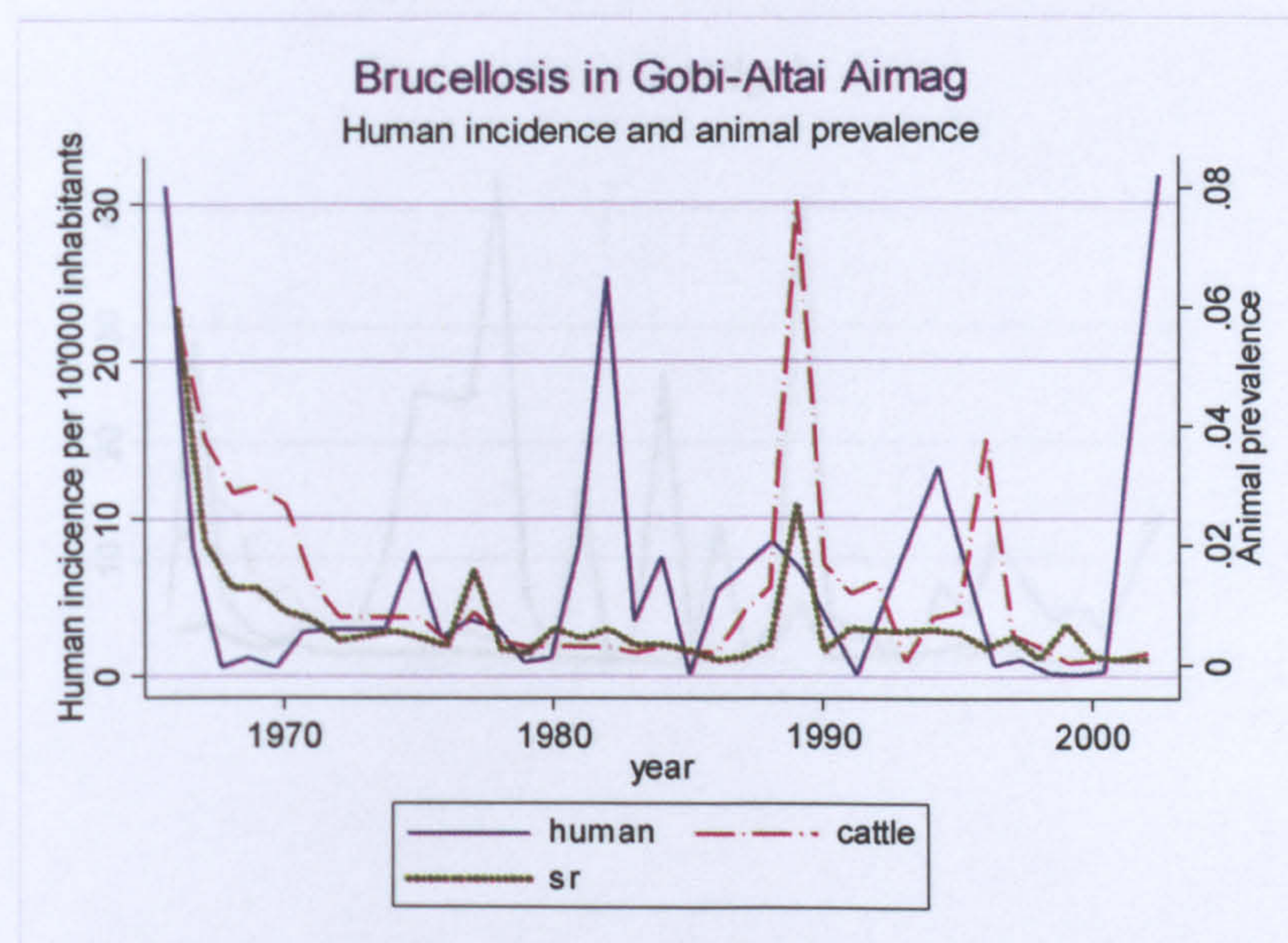
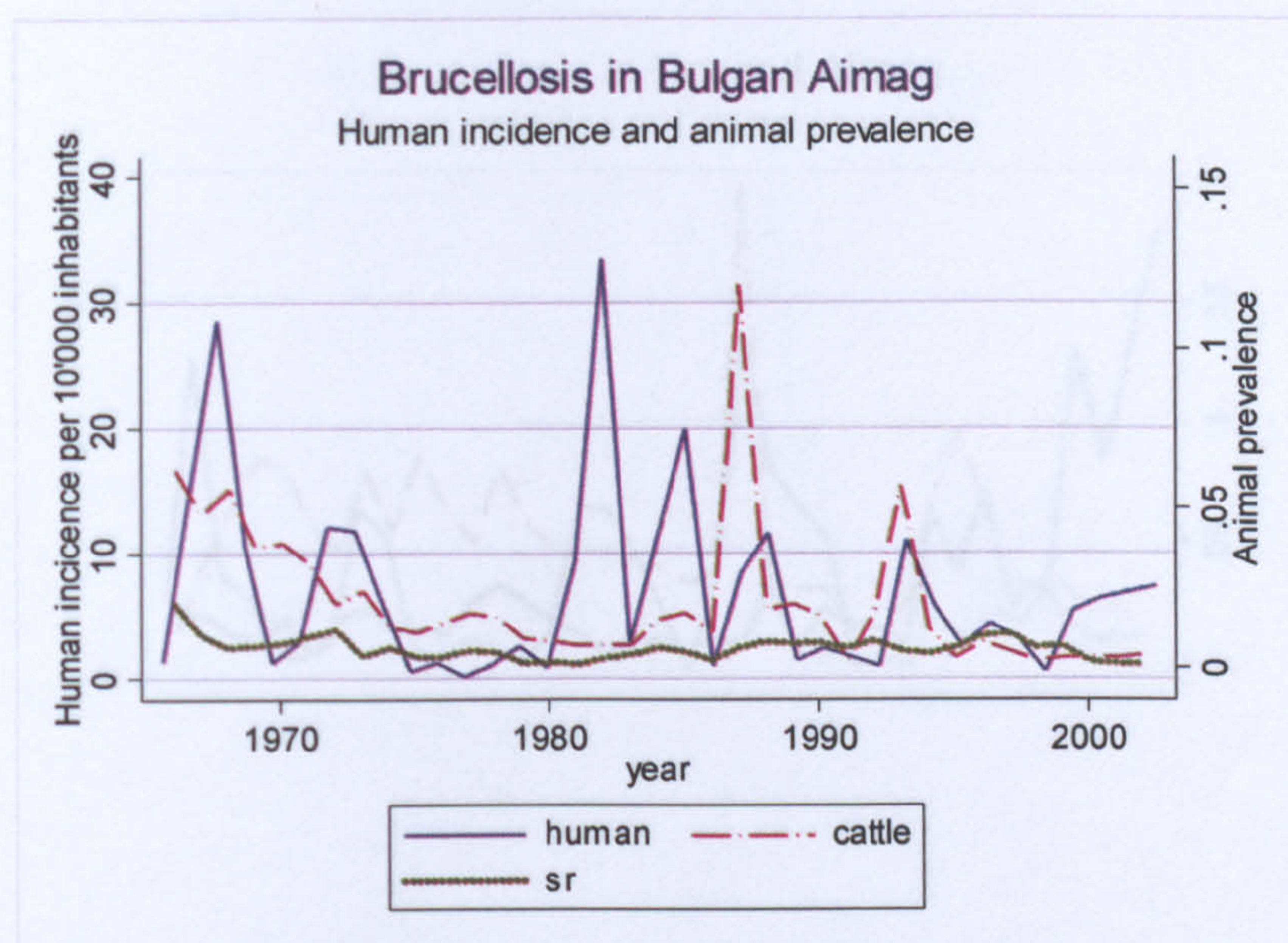
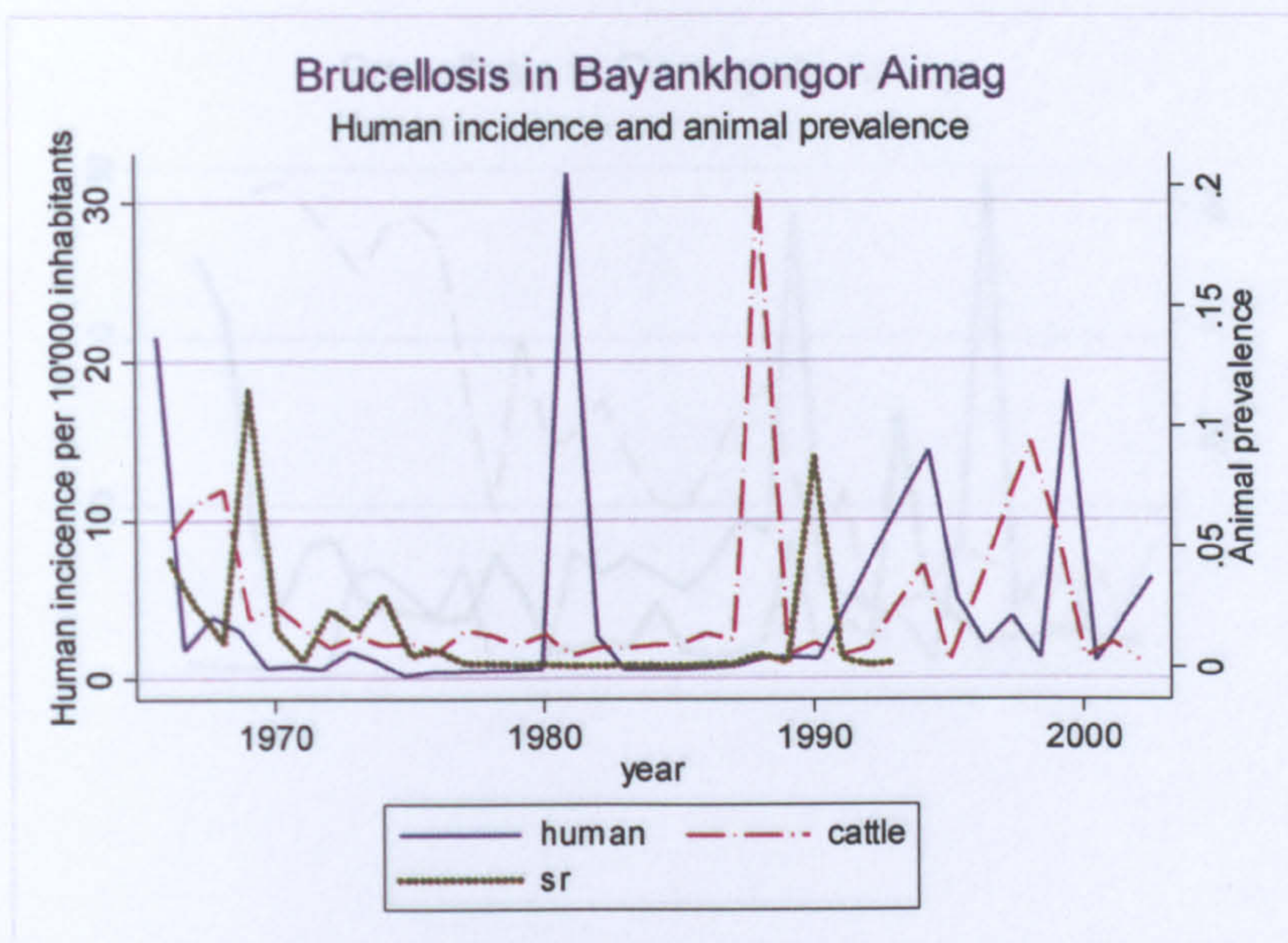
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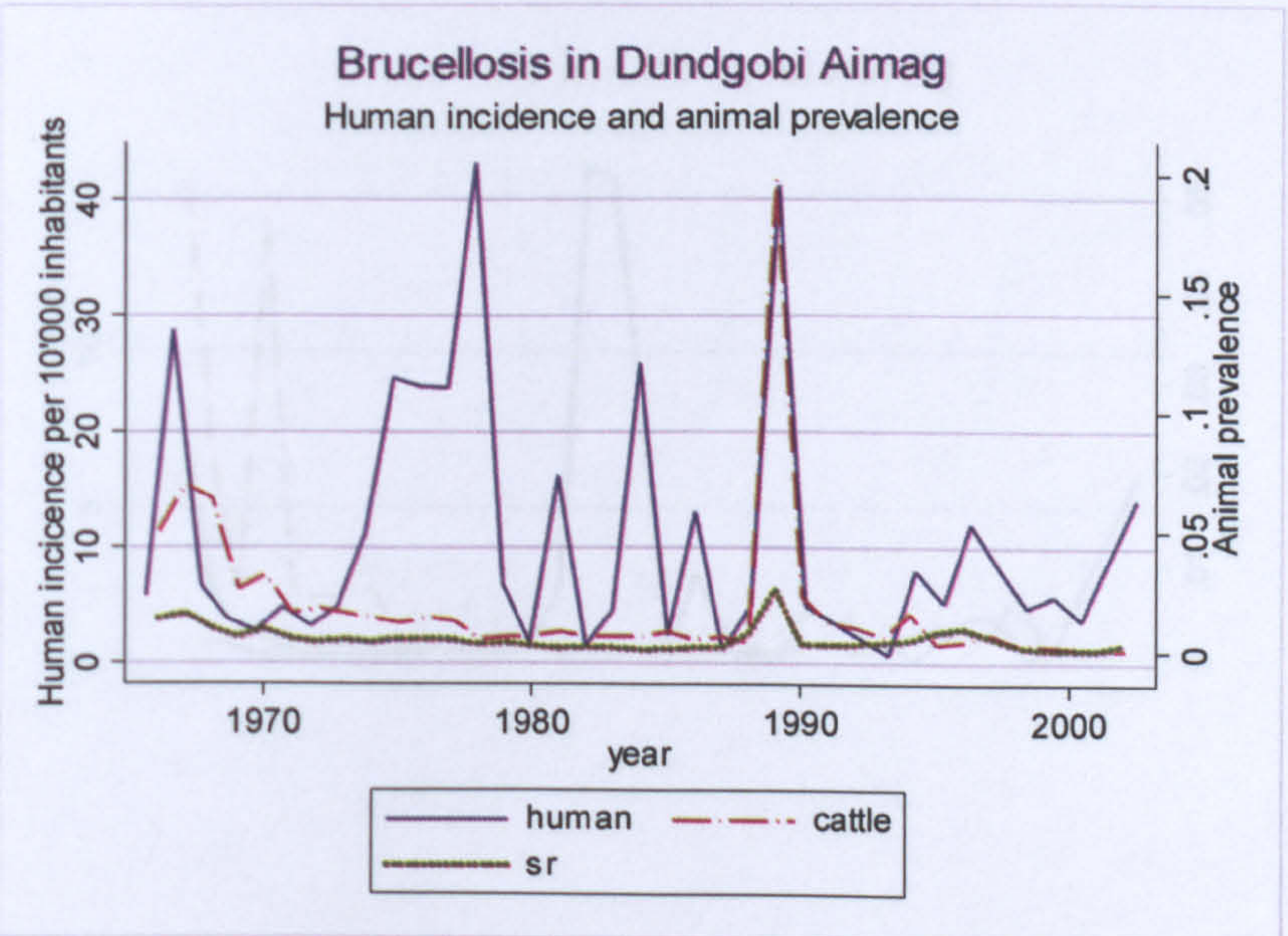
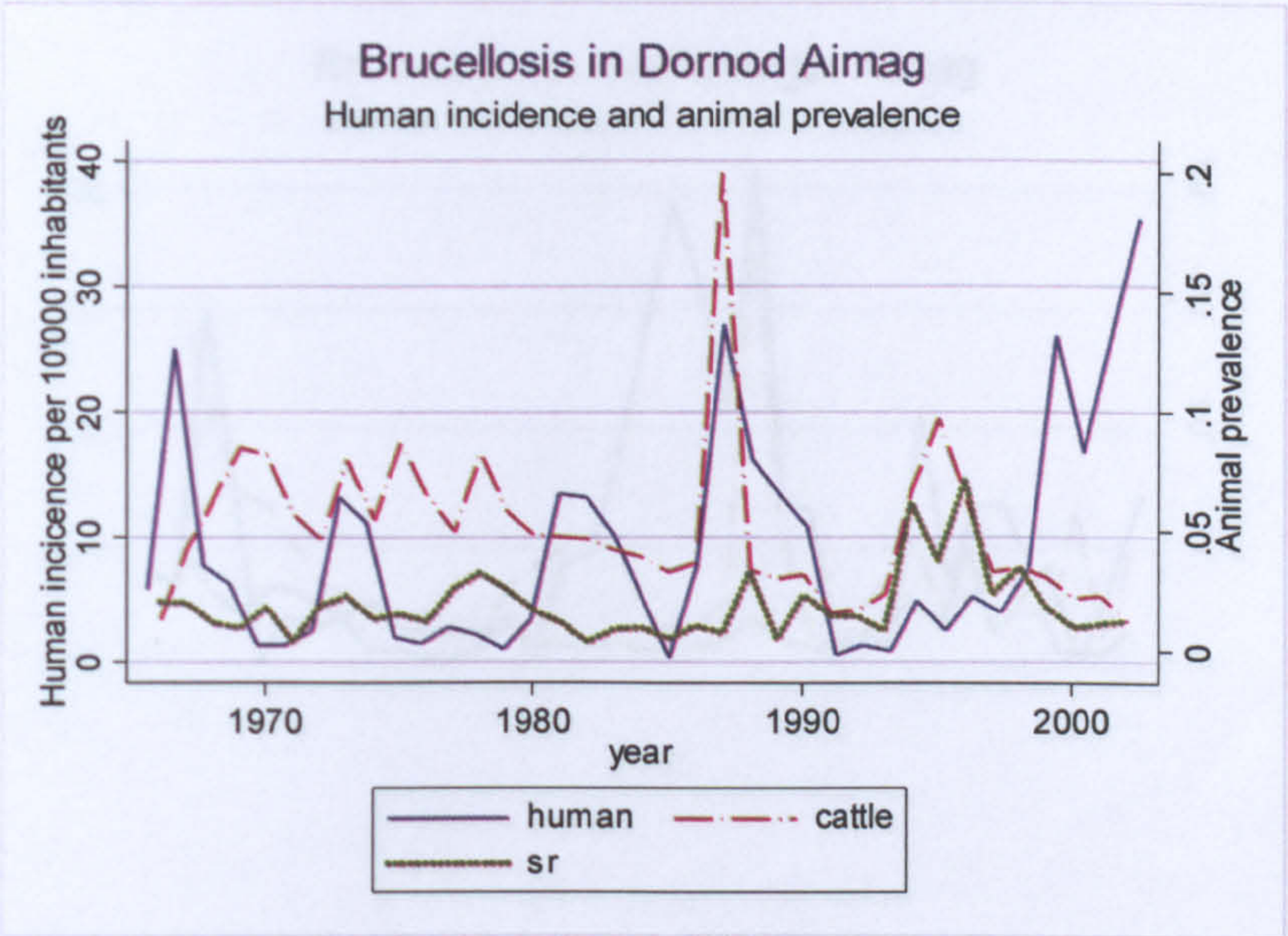
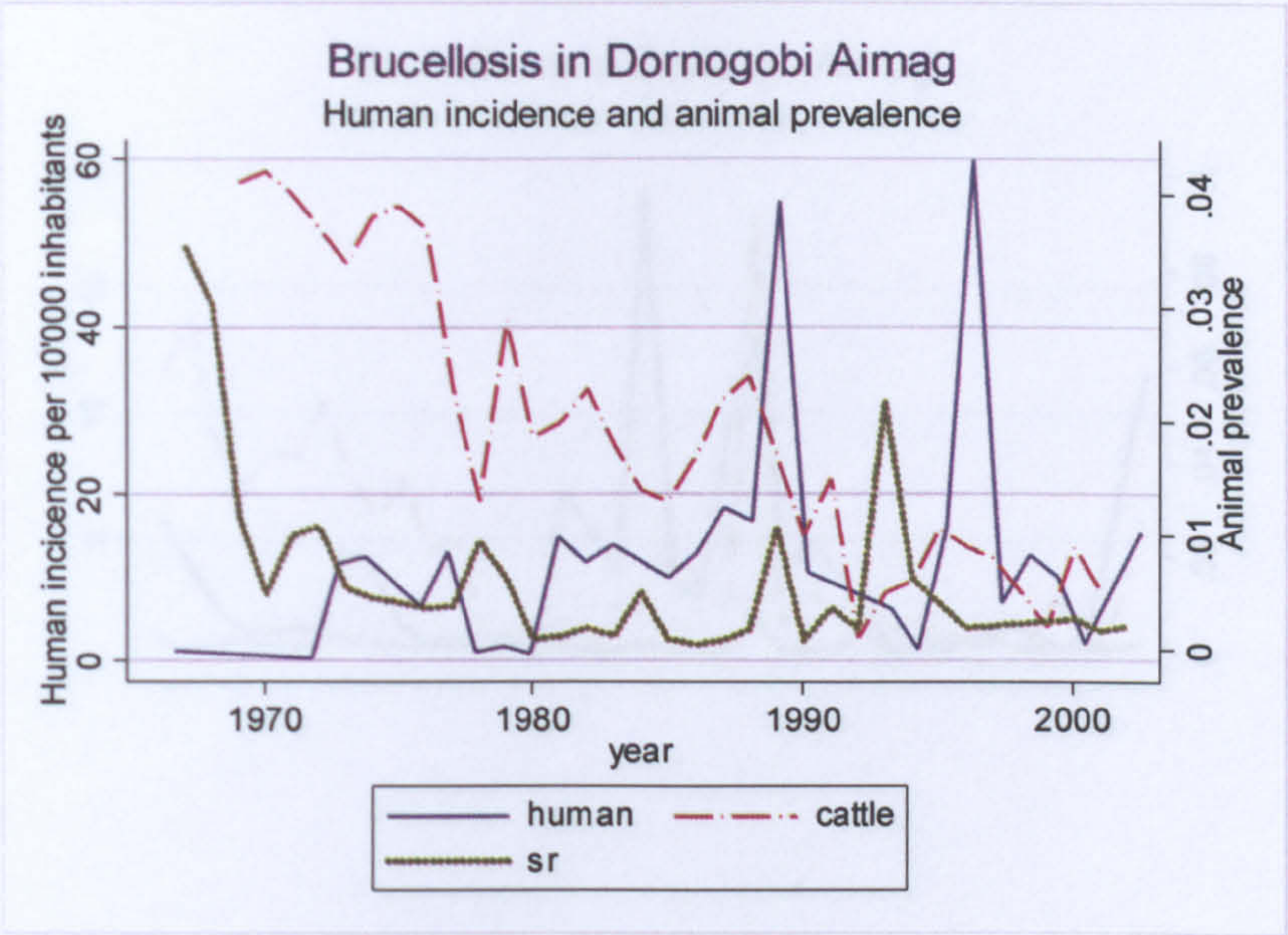


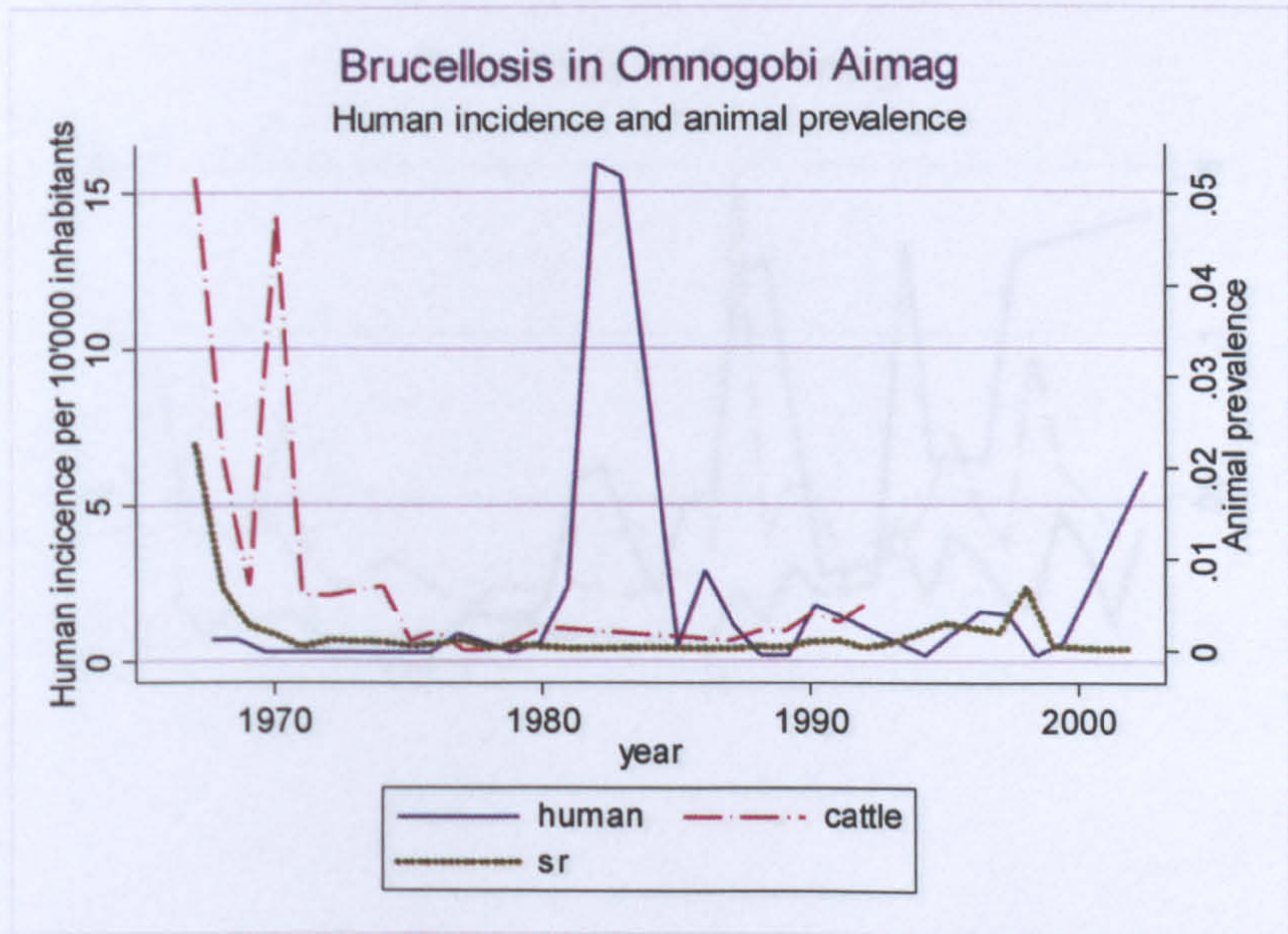
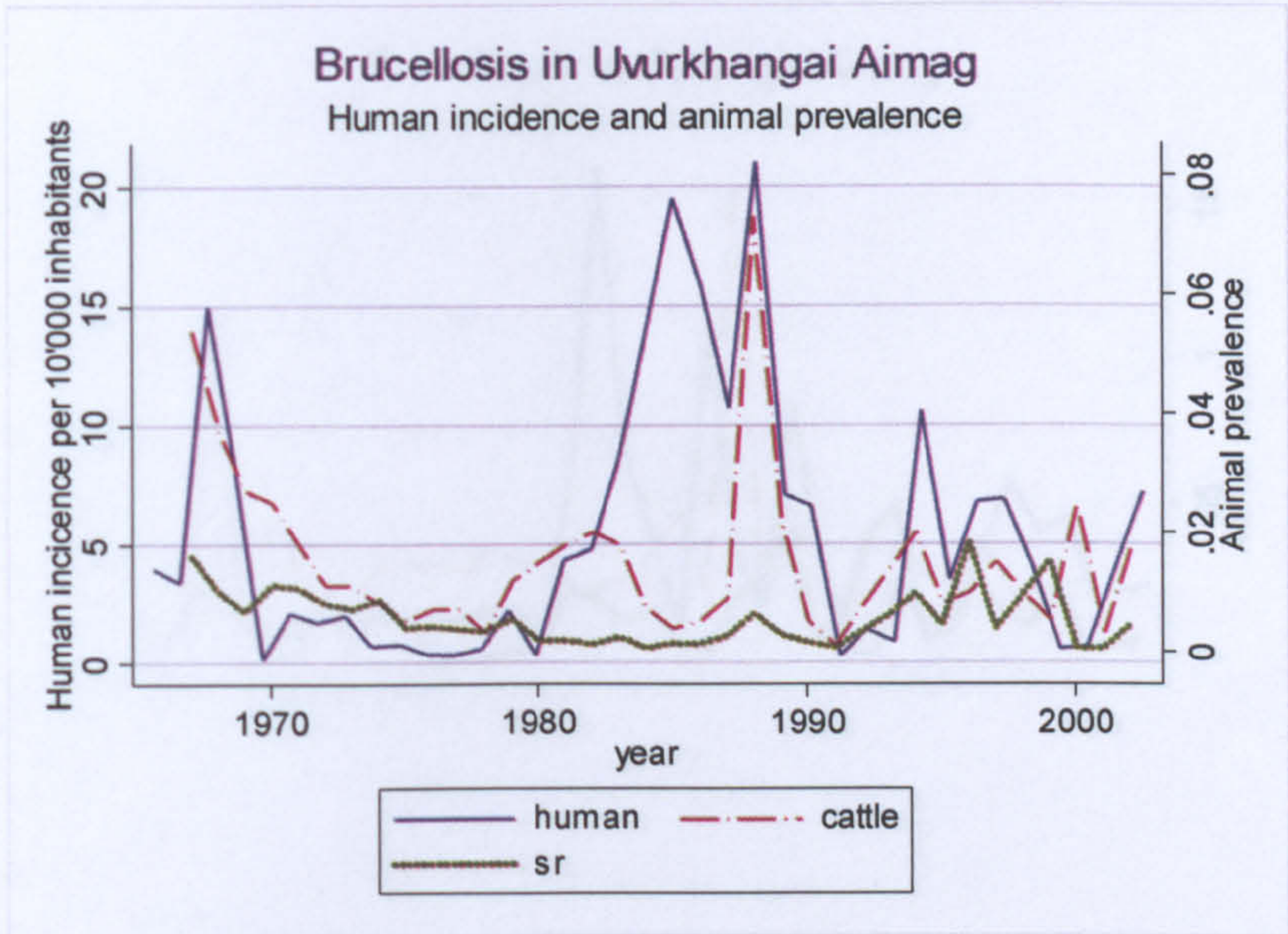
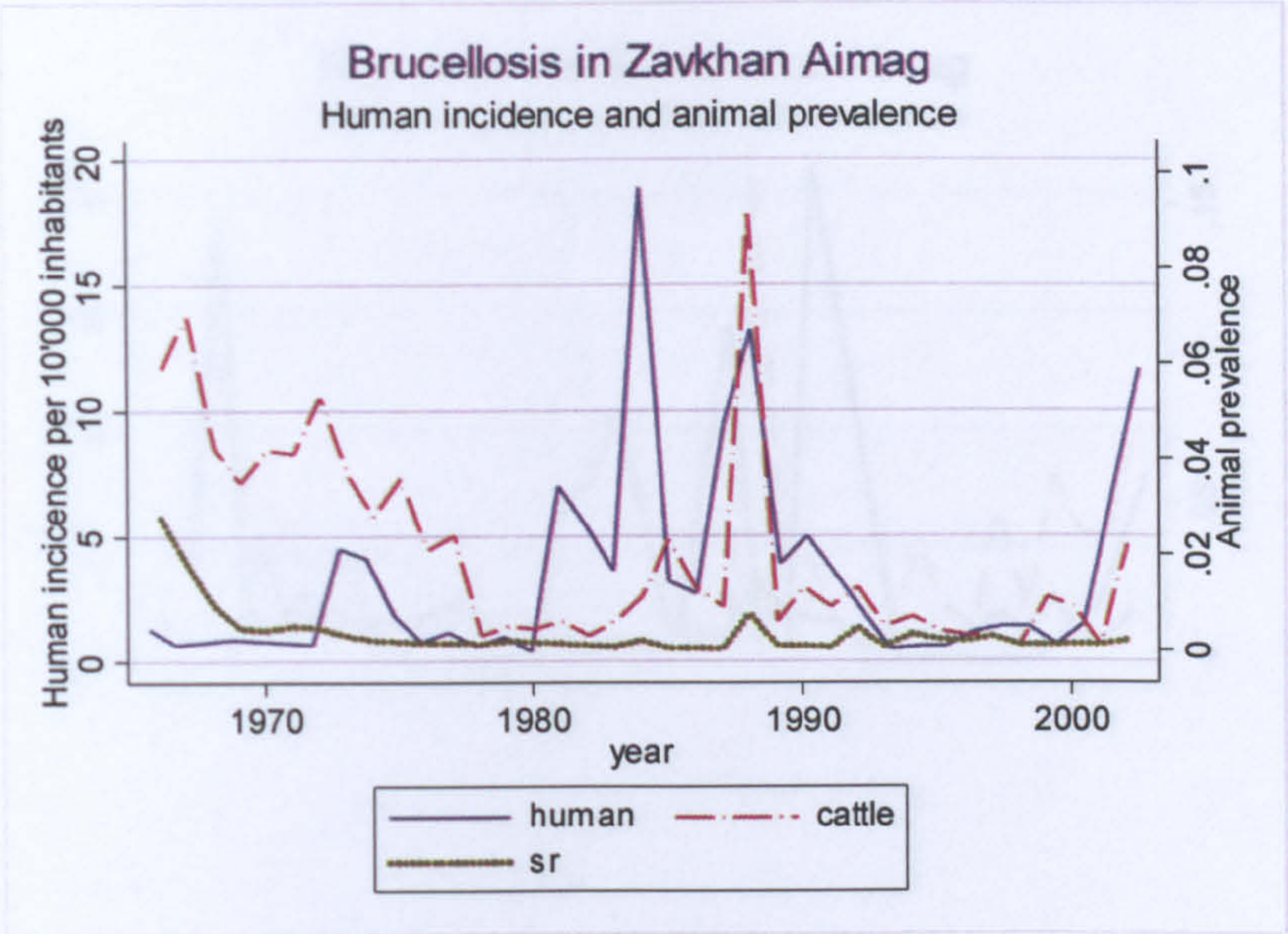
Appendix 4.2.: Brucellosis in Mongolia: human incidence and animal prevalence on Aimag level

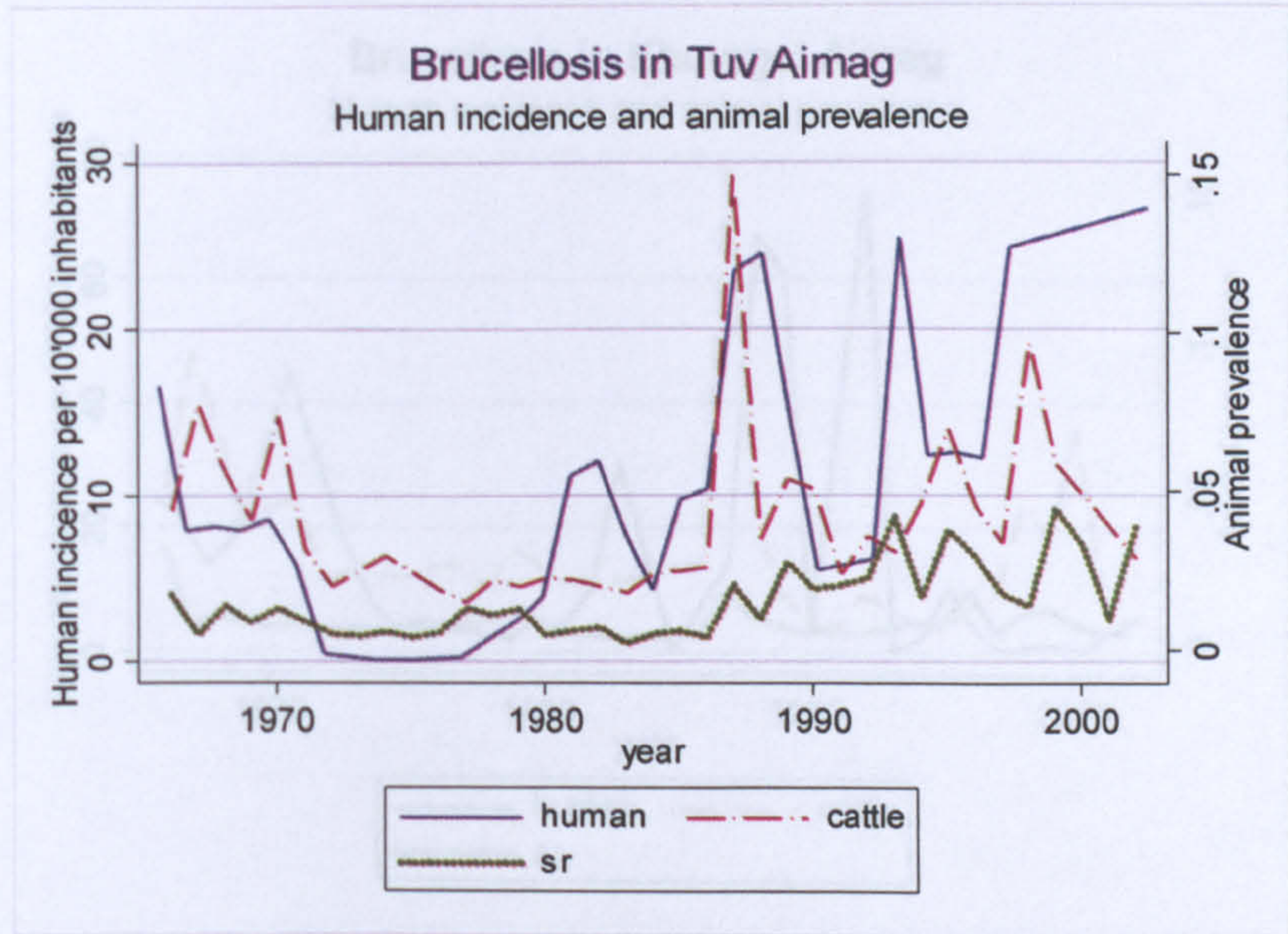
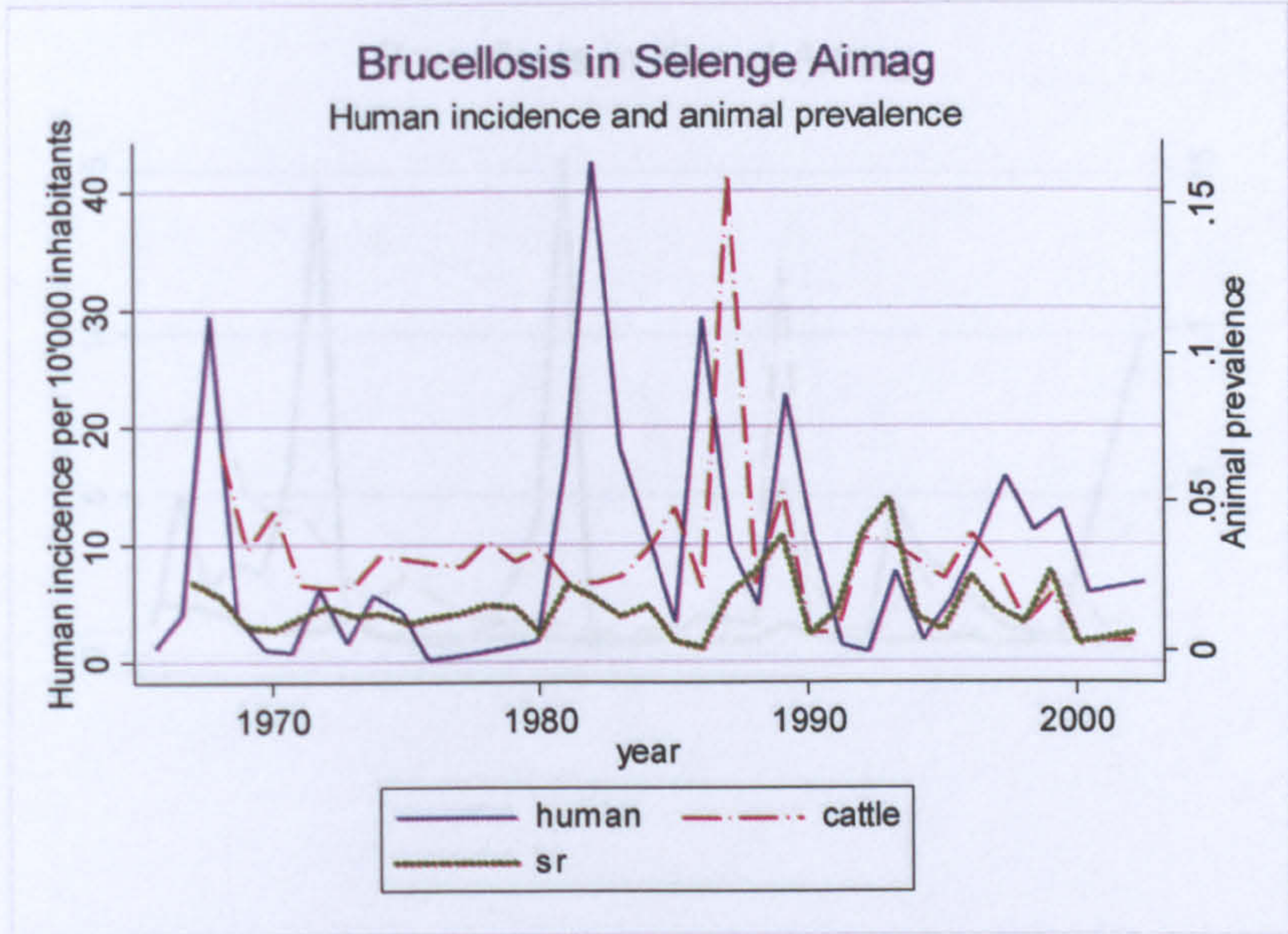
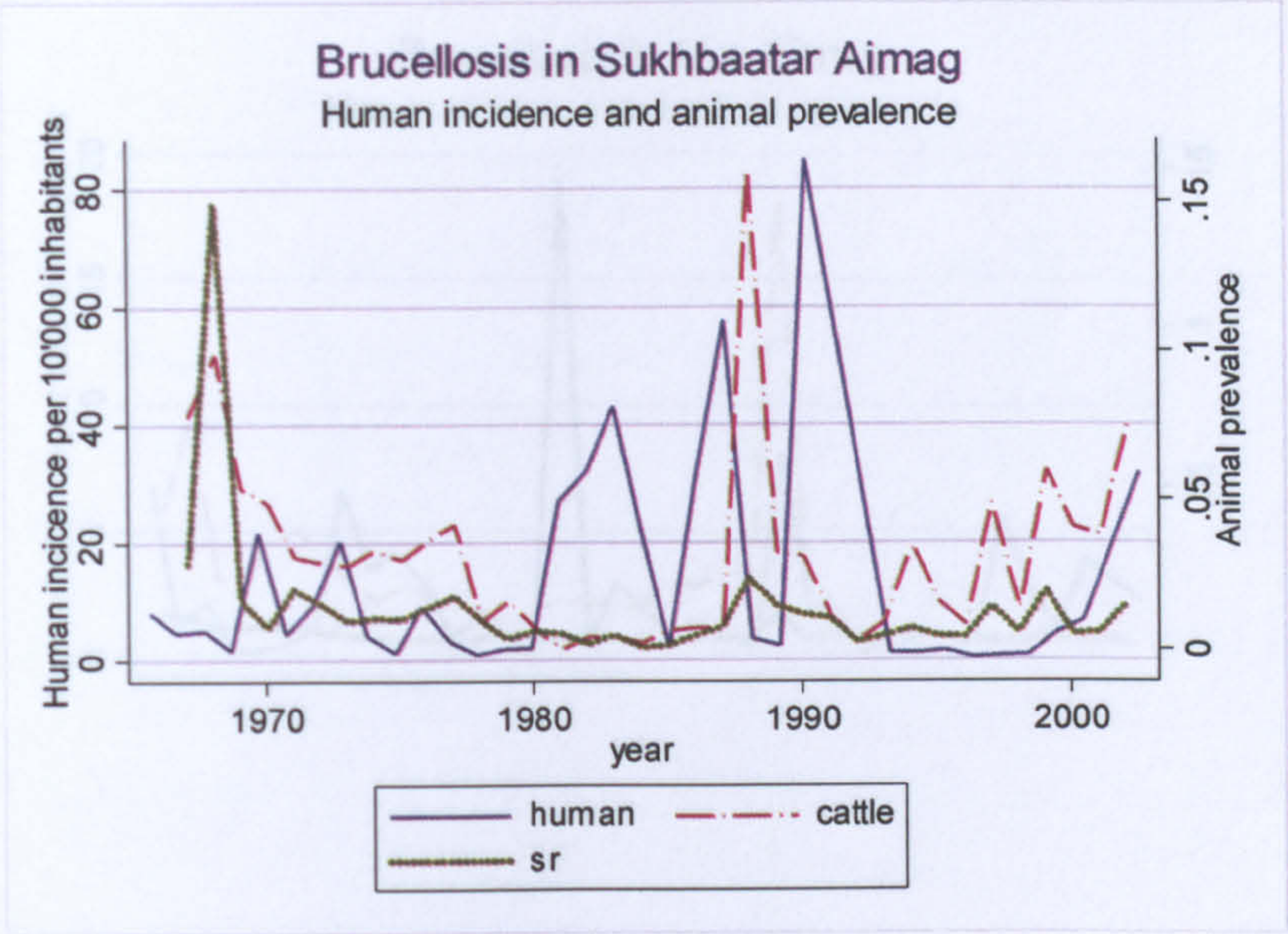
For every Aimag the incidence in humans and the prevalence in cattle and small ruminants are plotted on the same graph, for the time period 1966 to 2002. The data are derived from material collected for this thesis (*see chapter 3*).

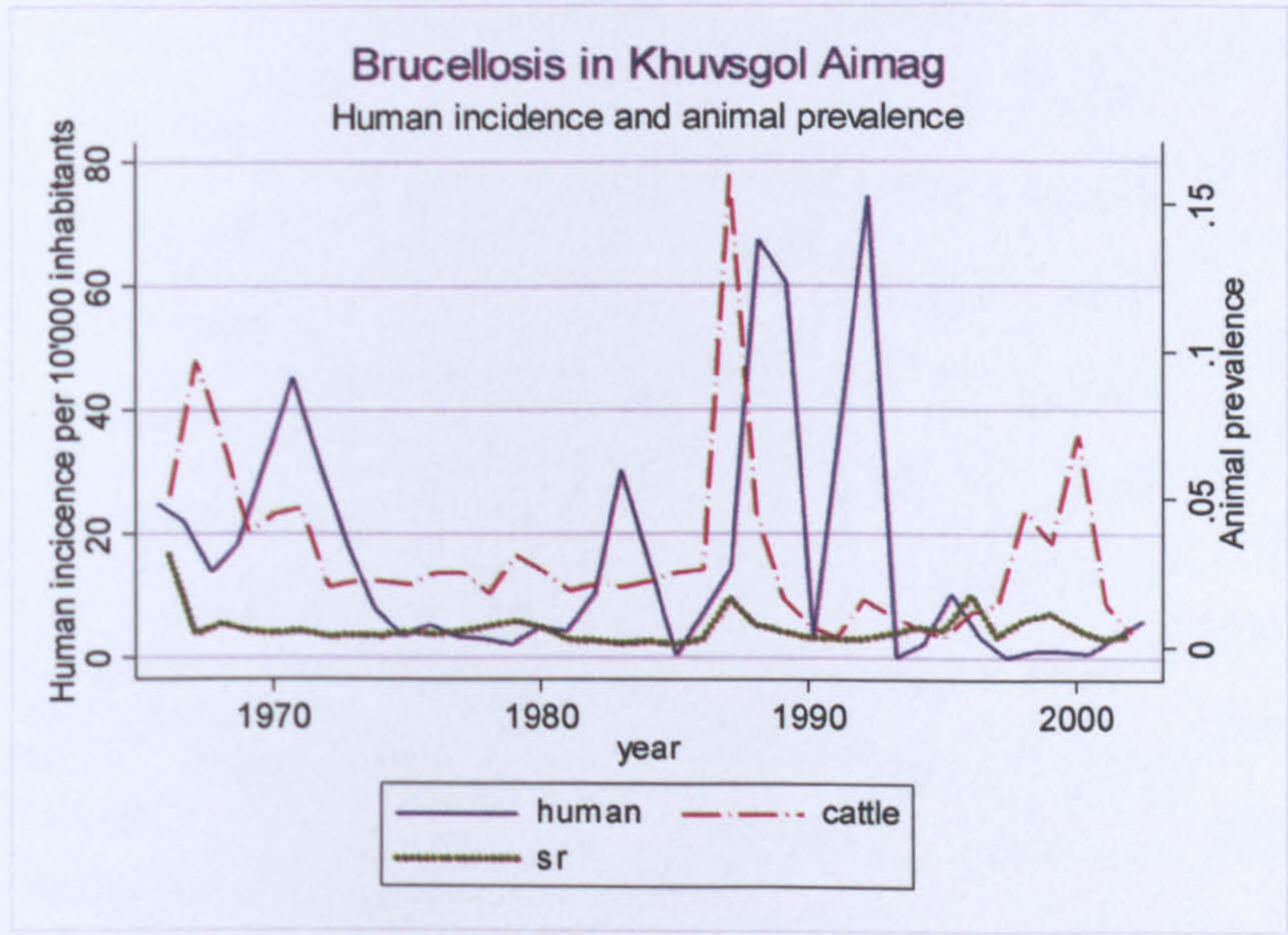
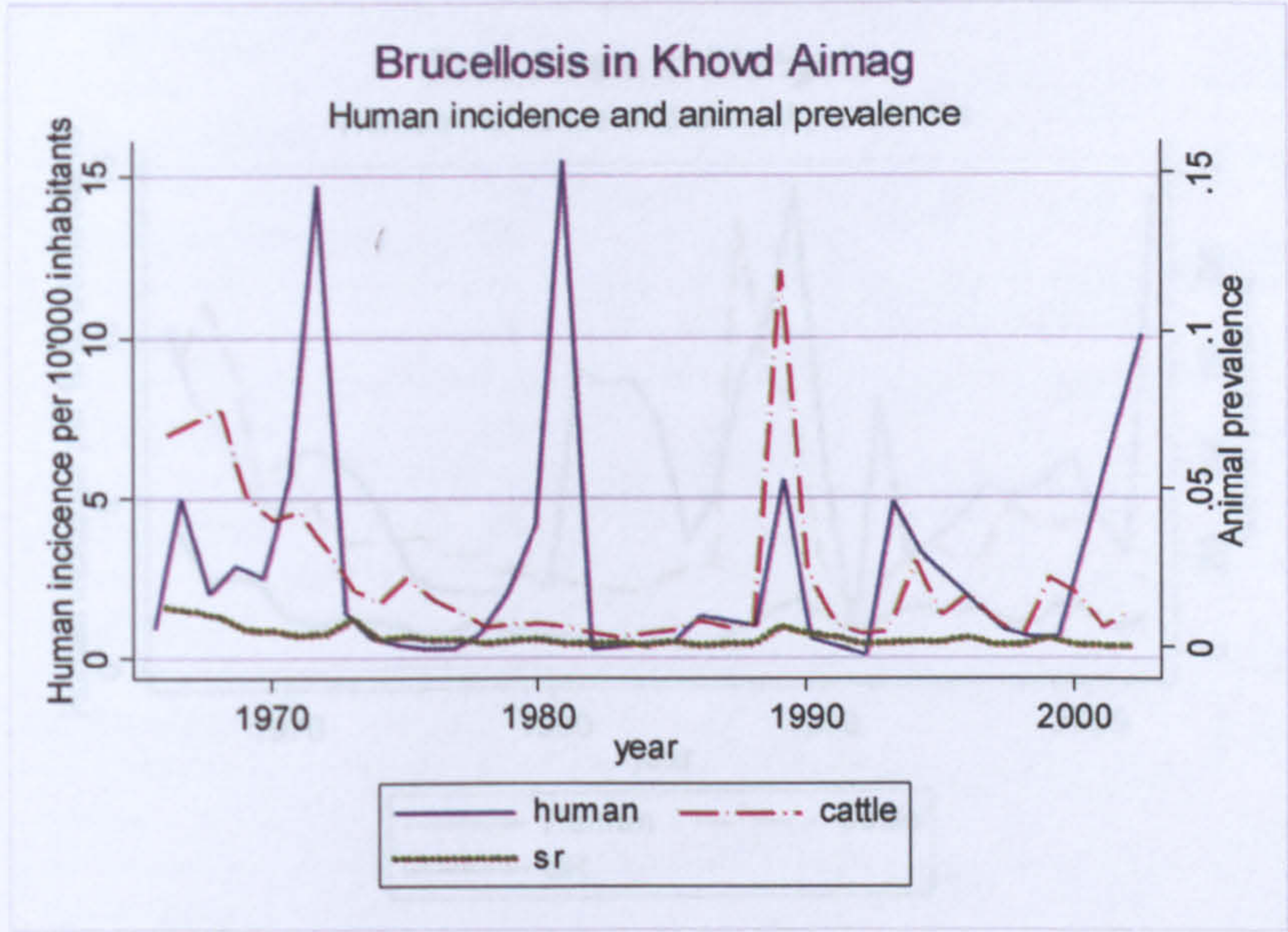
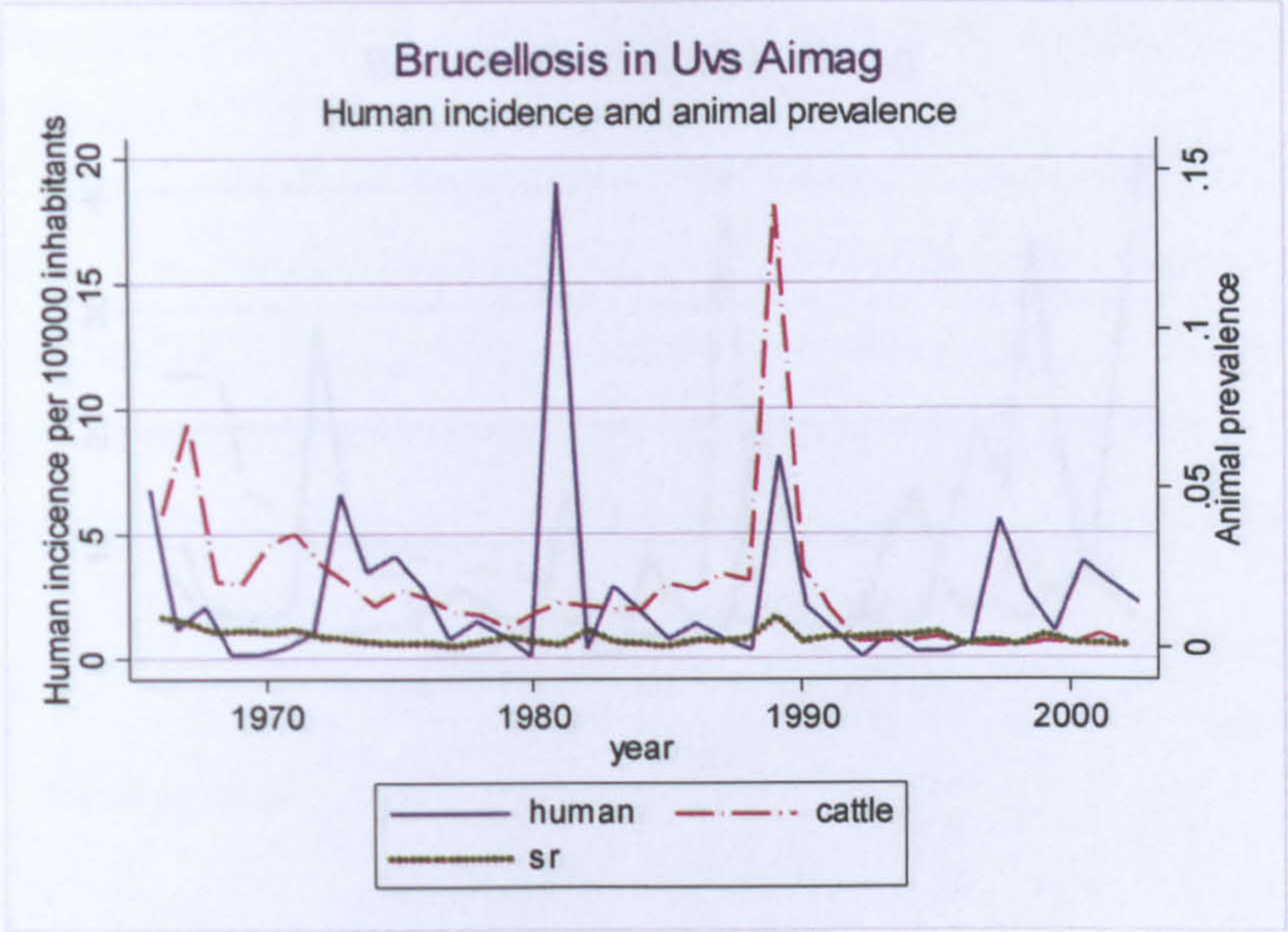


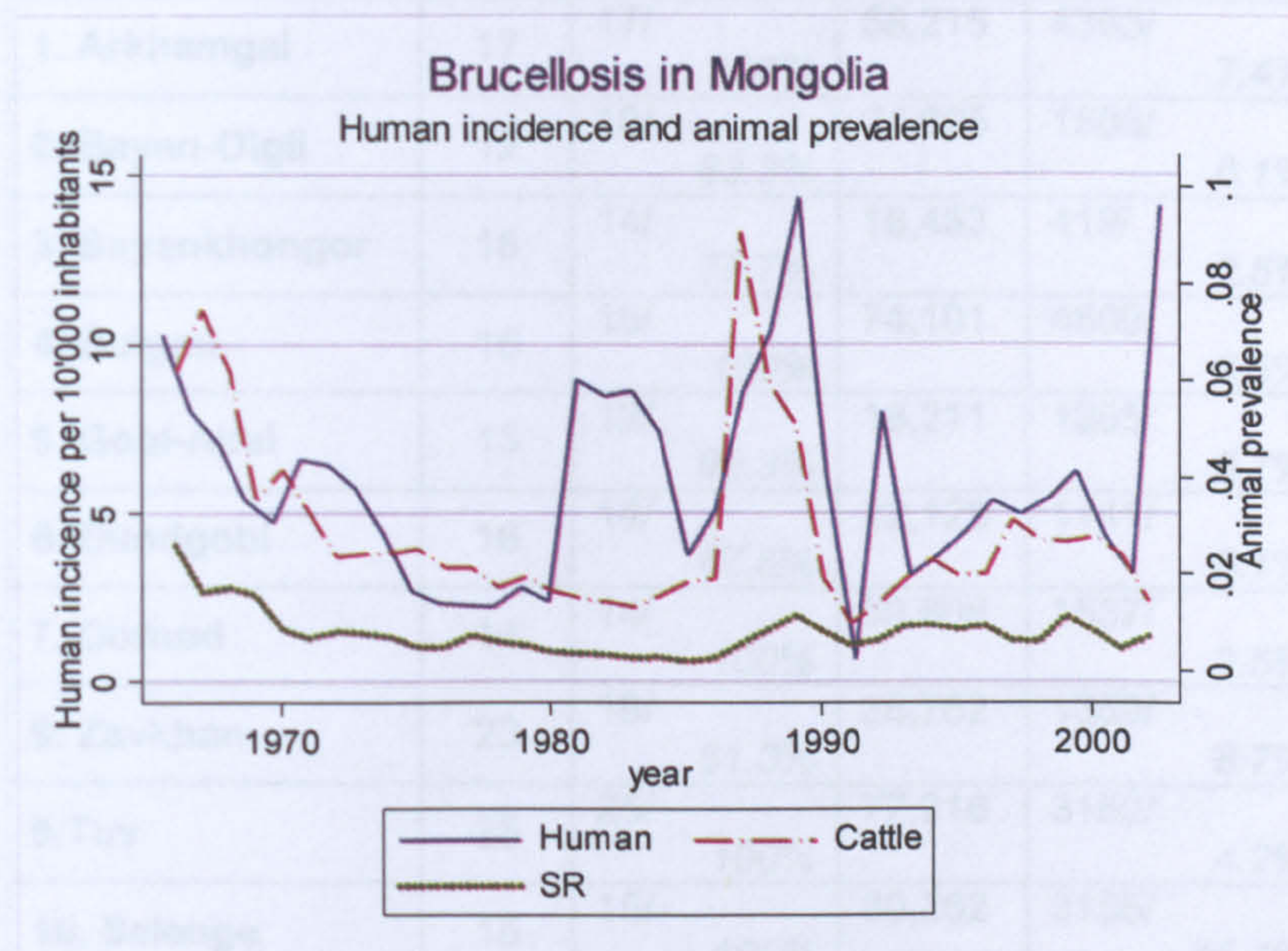
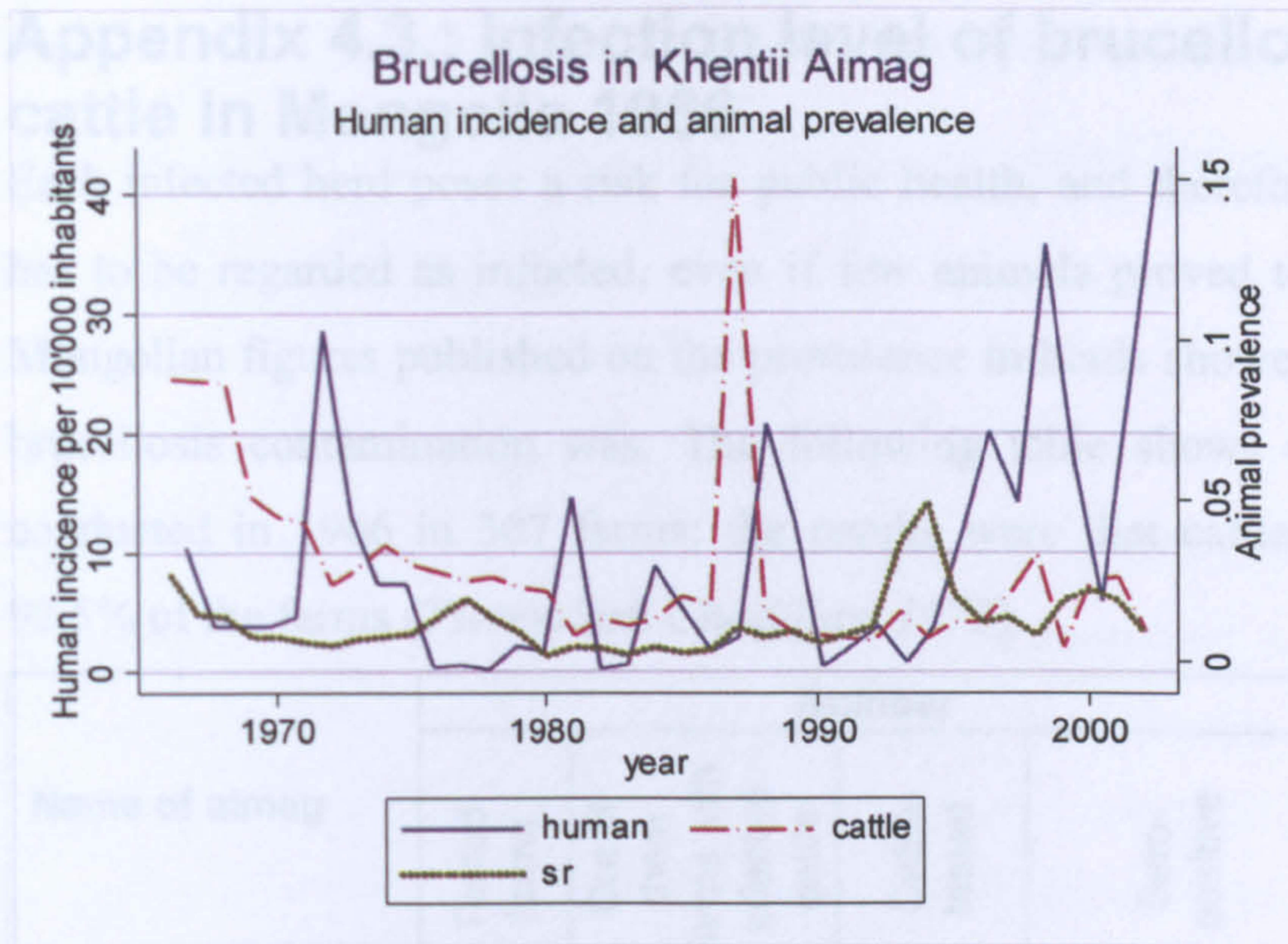












Appendix 4.3.: Infection level of brucellosis in cattle in Mongolia 1966

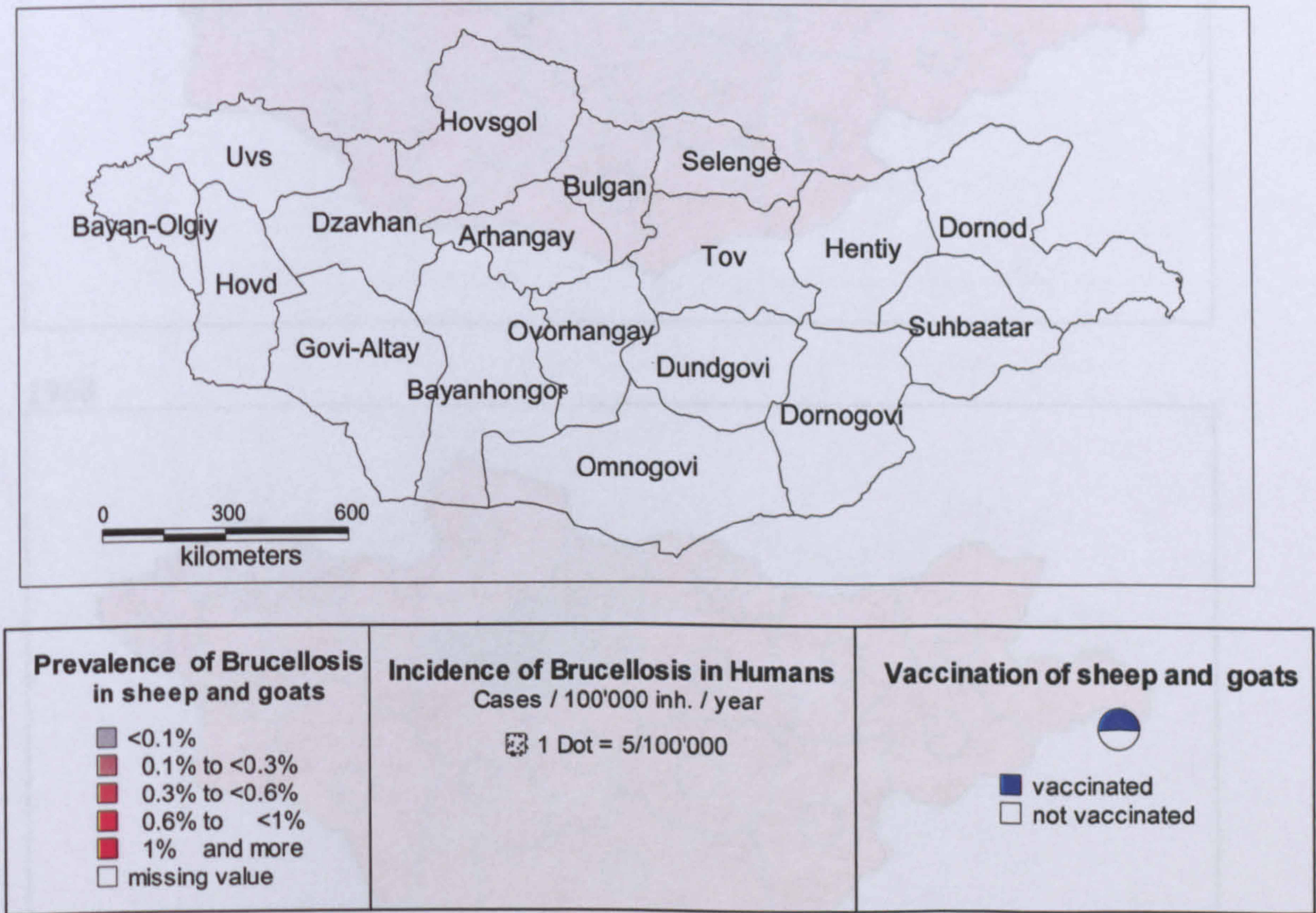
Each infected herd poses a risk for public health, and therefore the entire herd has to be regarded as infected, even if few animals proved to be seropositive. Mongolian figures published on the prevalence in herds showed how serious the brucellosis contamination was. The following table shows data on a survey conducted in 1966 in 307 farms: the results were that cattle were infected in 92.5% of the farms (*Tserendash Choijiljav, 1972*).

Name of aimag	Number			
	Tested farms	Out of them farms with infected cattle	Cattle tested	Sero-positive
1. Arkhamgai	17	17/ 100%	58,215	4363/ 7.4%
2. Bayan-Olgii	12	10/ 83.3%	24,695	1508/ 6.1%
3. Bayankhongor	18	14/ 77.7%	16,433	419/ 2.5%
4. Bulgan	16	16/ 100%	74,101	4869/ 6.5%
5. Gobi-Altai	13	12/ 92.3%	18,211	1255/ 6.7%
6. Dundgobi	16	14/ 87.5%	22,125	1141/ 5.1%
7. Dornod	14	14/ 100%	59,806	1537/ 2.5%
8. Zavkhan	23	19/ 81.3%	36,762	1359/ 8.7%
9. Tuv	25	25/ 100%	77,216	3180/ 4.2%
10. Selenge	15	15/ 100%	30,262	3155/ 10.4%
11. Uvs	17	17/ 100%	44,893	1607/ 3.5%
12. Khovd	14	10/ 71.4%	24,190	1546/ 6.3%
13. Khuvsgul	25	25/ 100%	72,929	3701/ 5.07%
14. Khentee	20	20/ 100%	10,209 8	9531/ 9.3%
15. Sukhbaatar	14	14/ 100%	51,377	4091/ 7.9%
16. Uvurkhangai	19	16/ 84.2%	87,232	5371/ 6.1%
17. Dornogobi	15	15/ 100%	16,527	2145/ 12.9%
18. Umnogobi	15	11/ 73.3%	7768	344/ 4.4%
Total	307	284/ 92.5%	824,840	51,102/ 6.1%

(*Tserendash Choijiljav, 1972*)

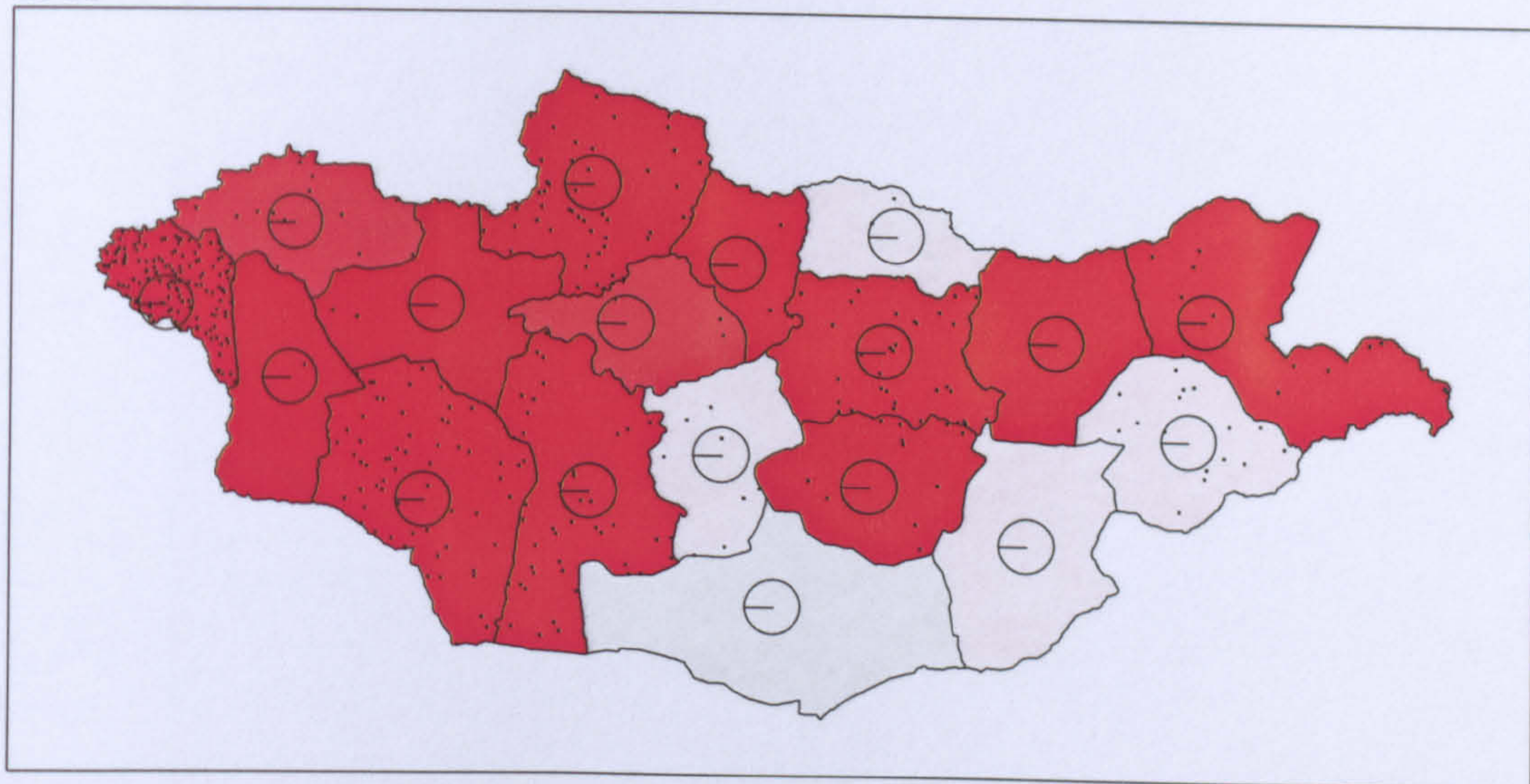
Appendix 5.1.: Brucellosis incidence in humans, prevalence in small ruminants, and immunisation in small ruminants

Brucellosis incidence in humans is shown, together with the prevalence in SR and the immunisation process in SR, with a geographical information system (*GIS Mapinfo software*). The template map of Mongolia has been downloaded from internet². The territory covered by the immunisation process expanded gradually from 1975 onwards; every year additional Aimags were added to the programme, until 1980, when all female SR were immunised nationwide. One notices the success of this campaign, and while it lasted, the prevalence of brucellosis in SR was generally lowered nationally (*see chapter 5*). The data are derived from material collected for this thesis (*see chapter 3*).



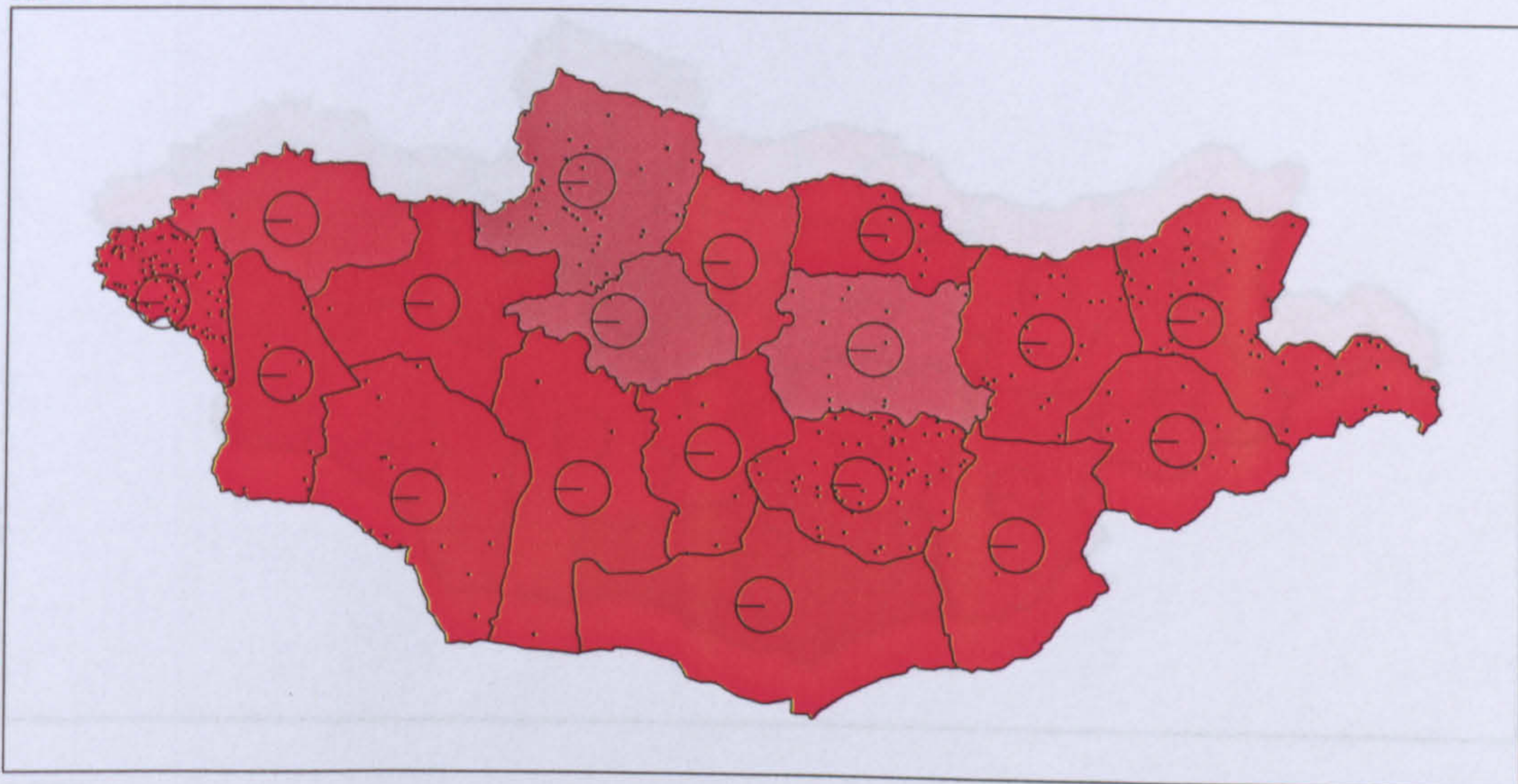
² <http://www.cipotato.org/DIVA/data/DataServer.htm>

1966



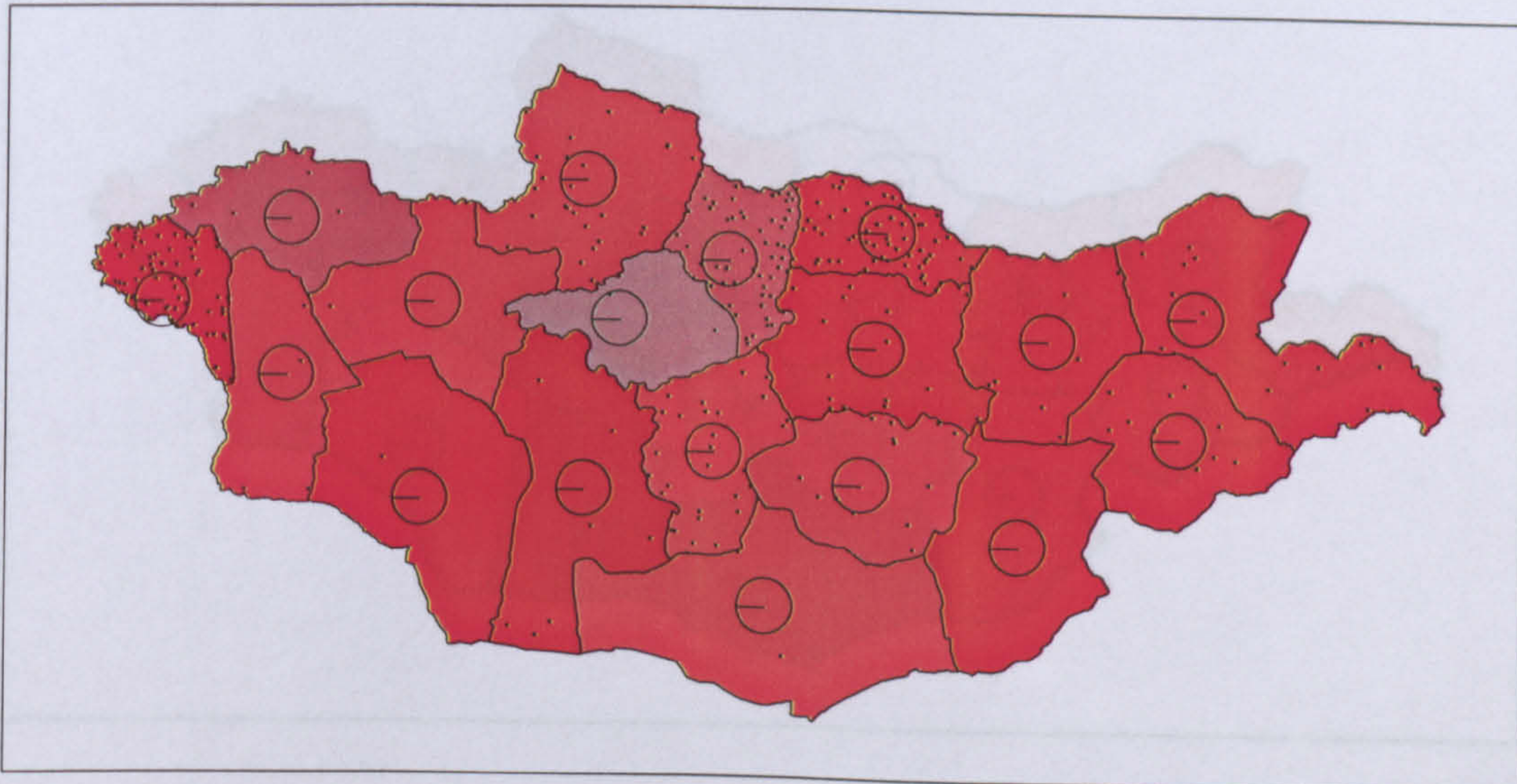
1978

1967

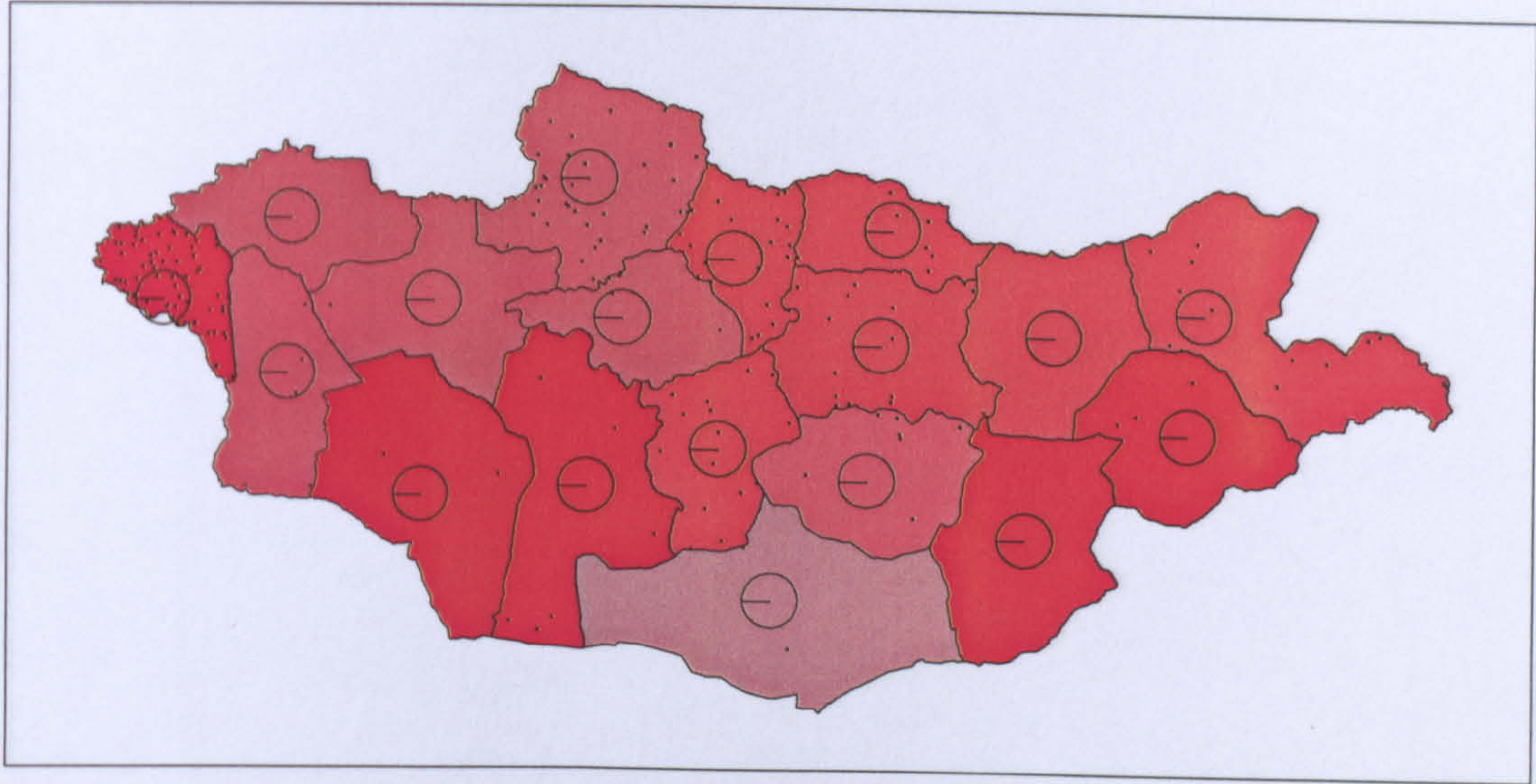


1971

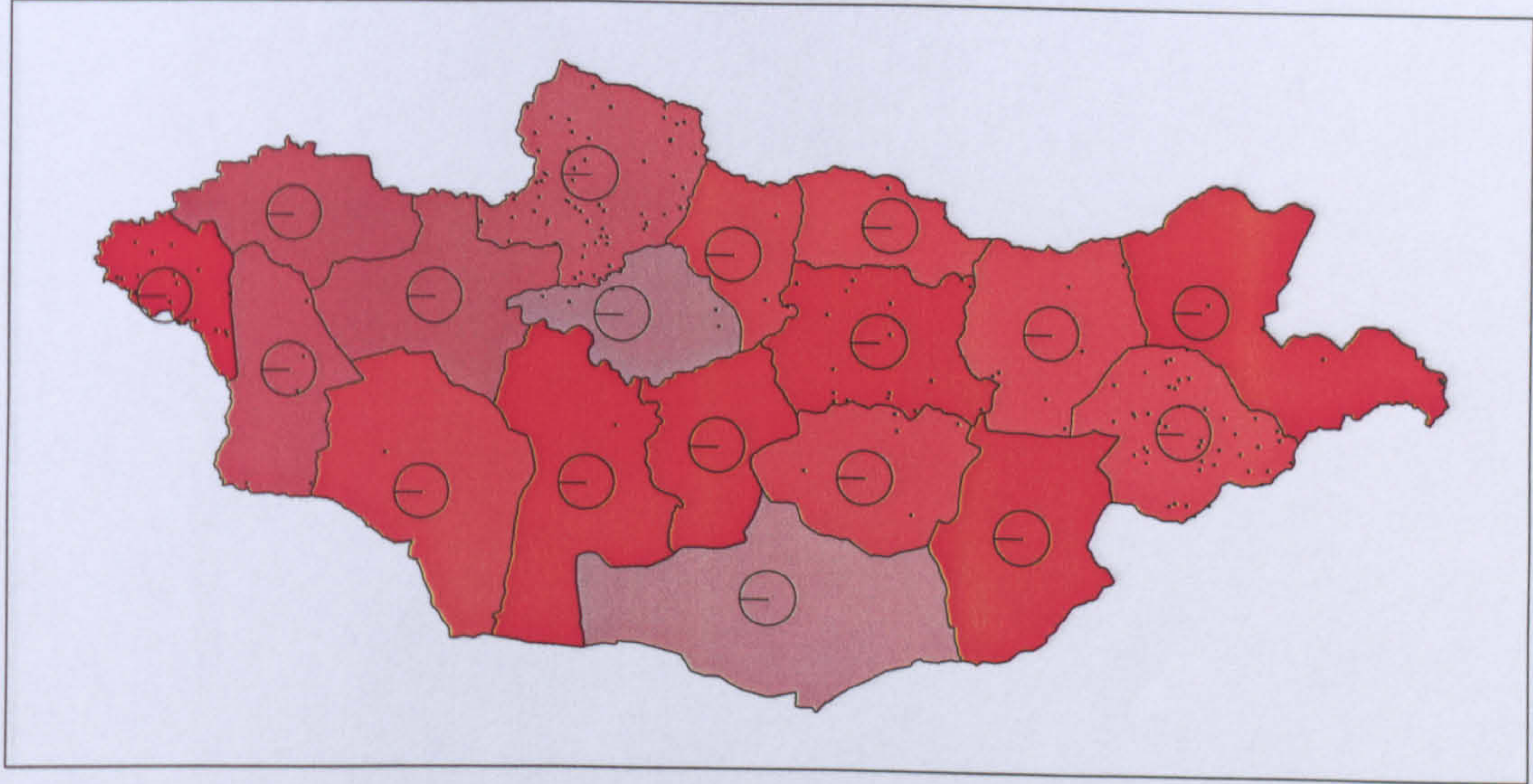
1968



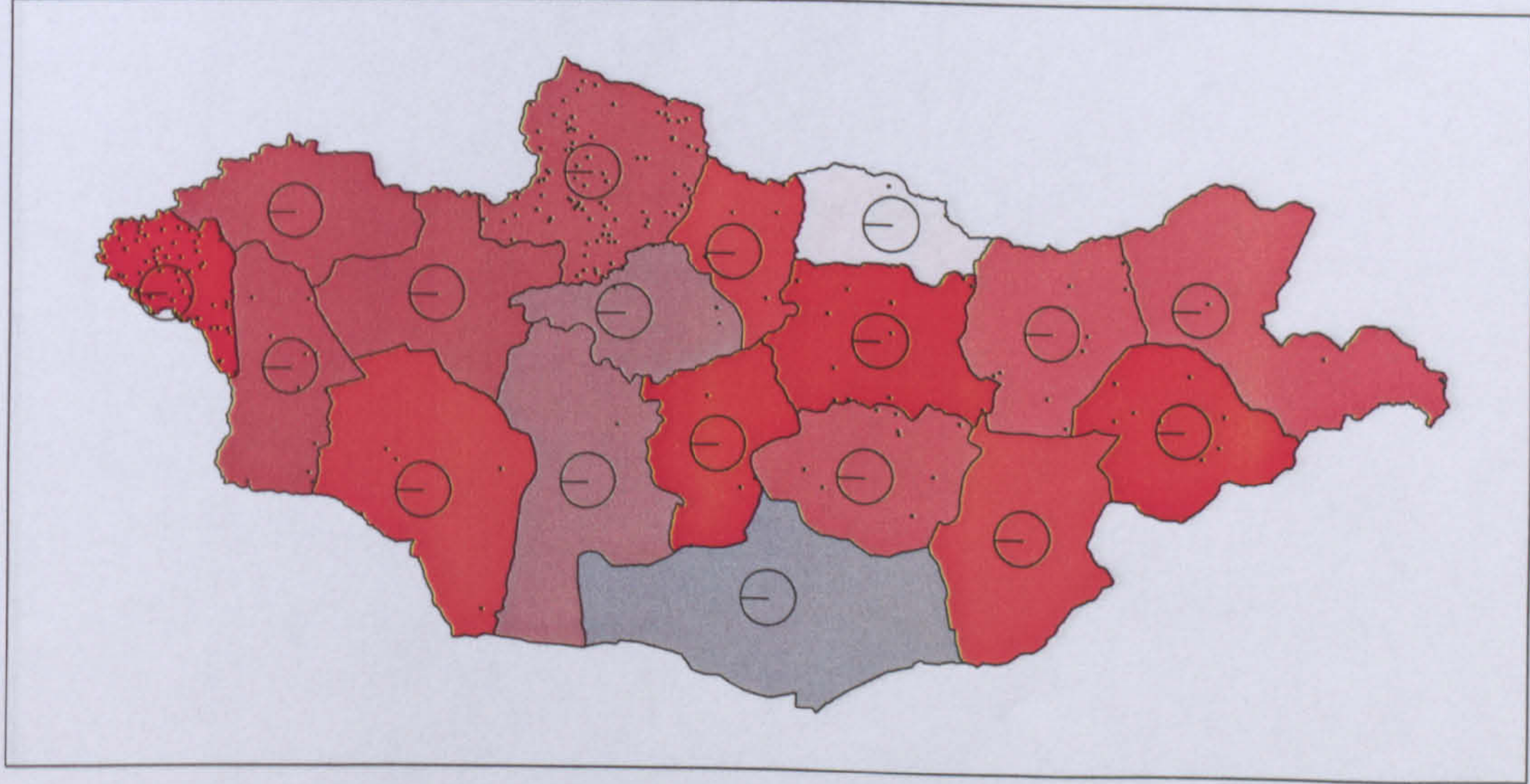
1969



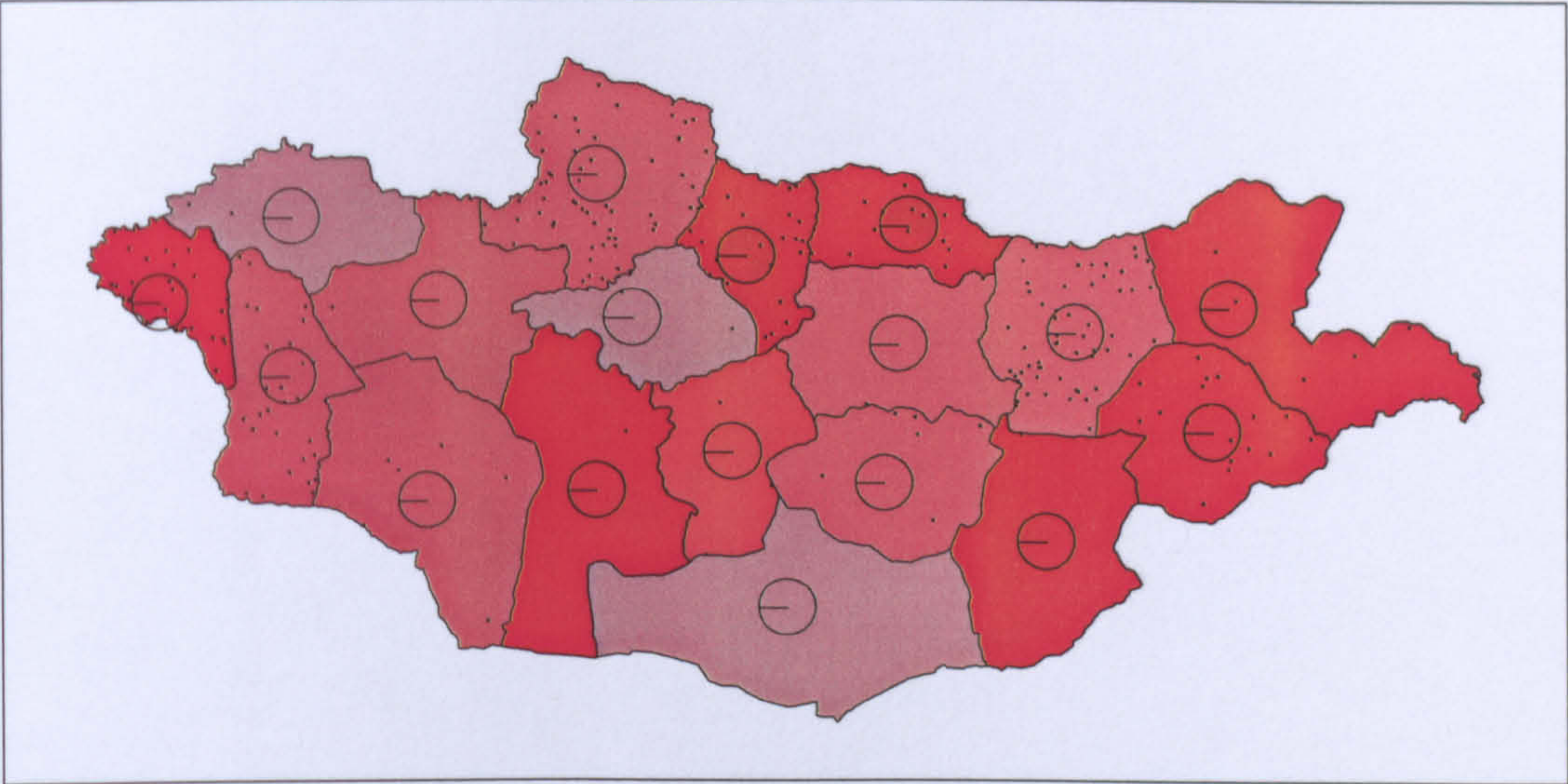
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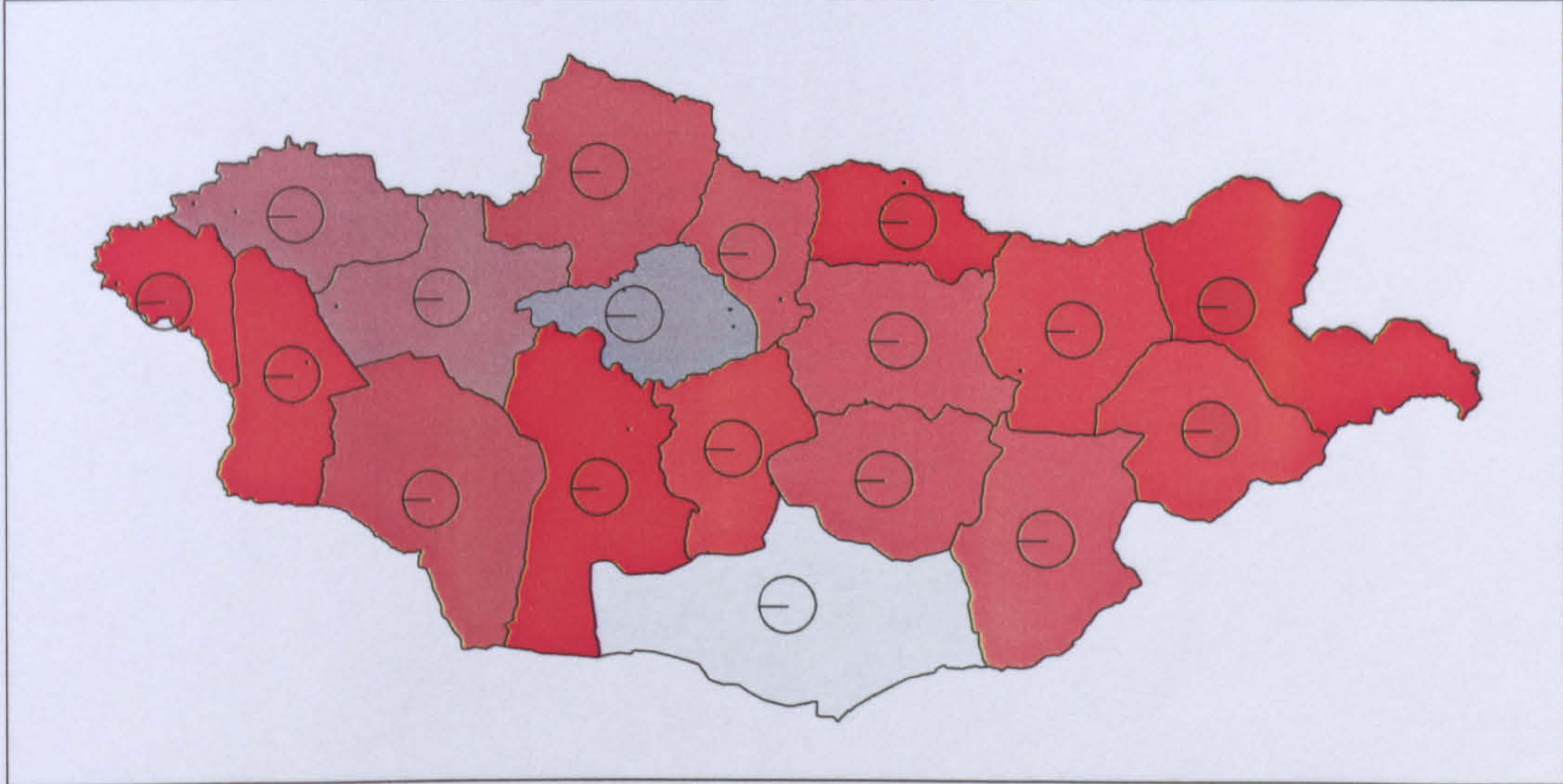
1971



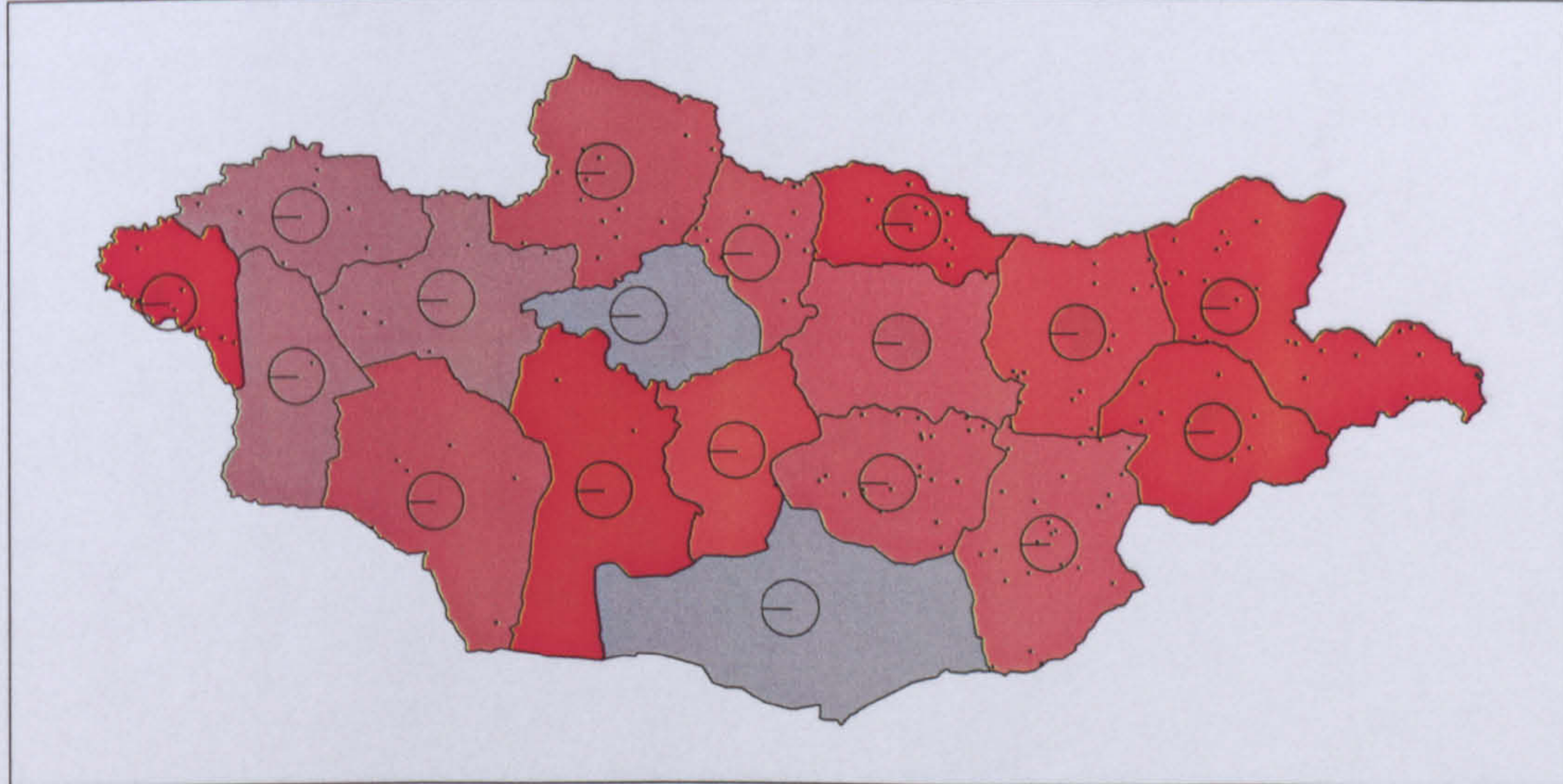
1972



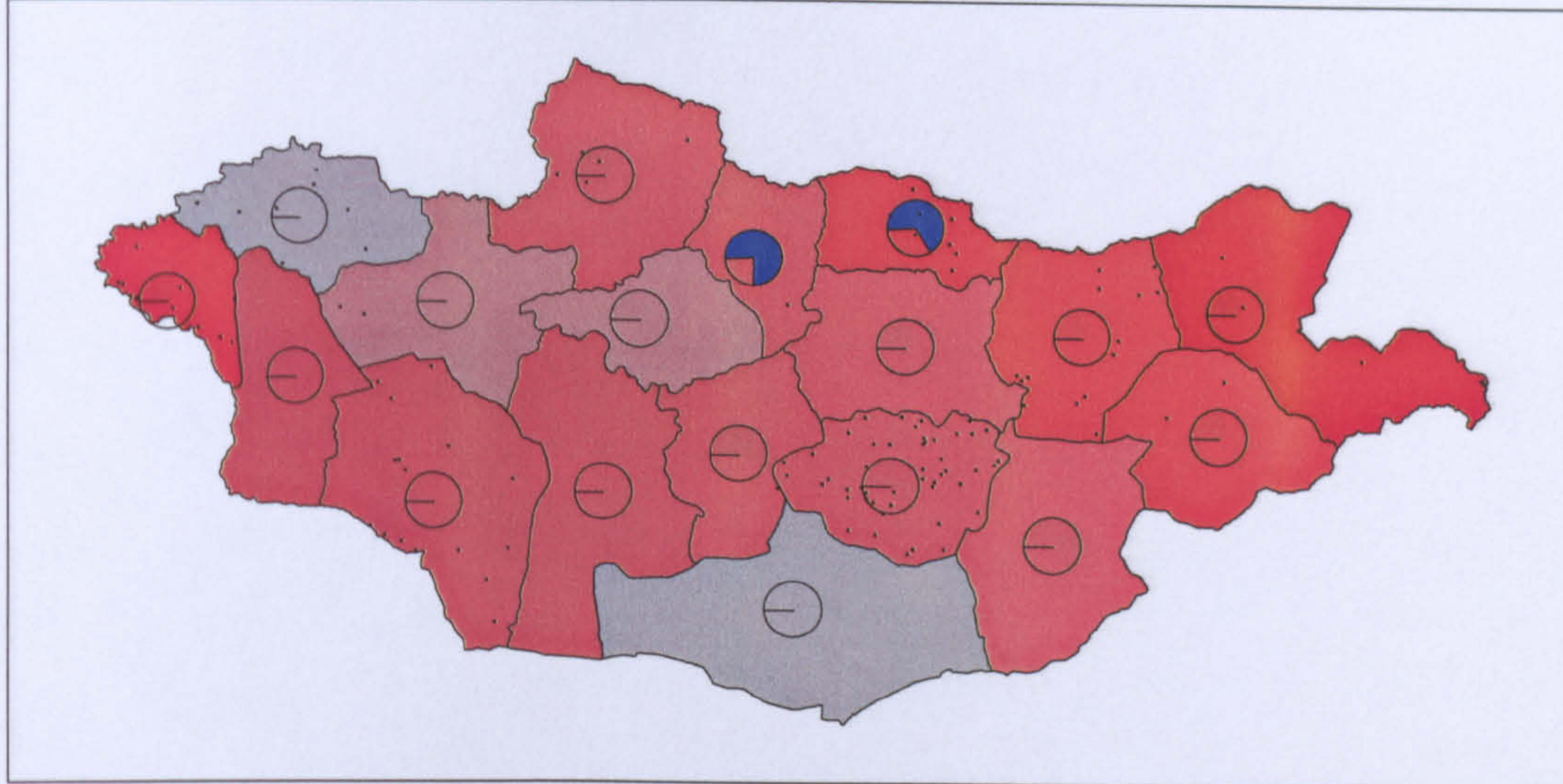
1973



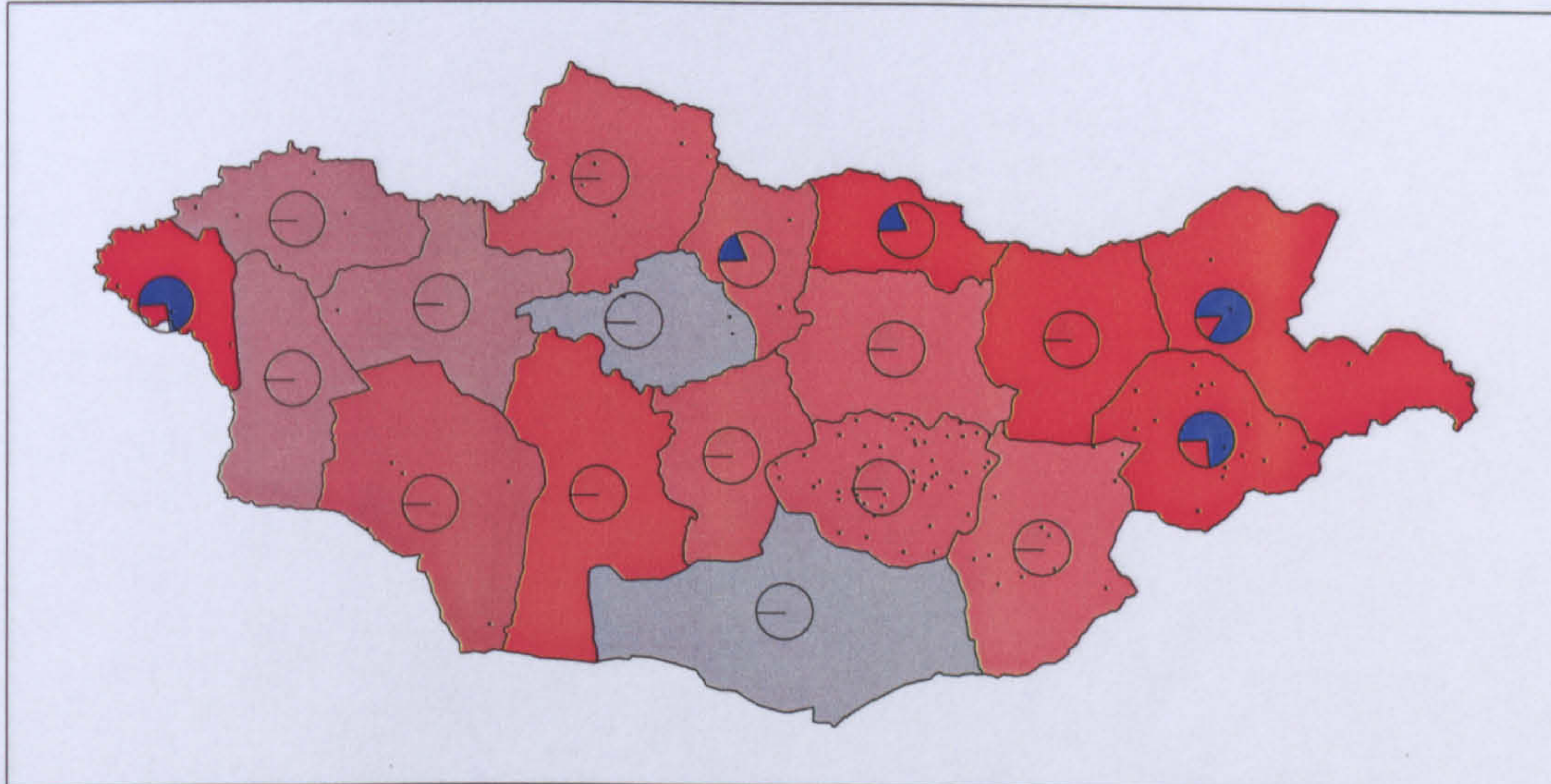
1974



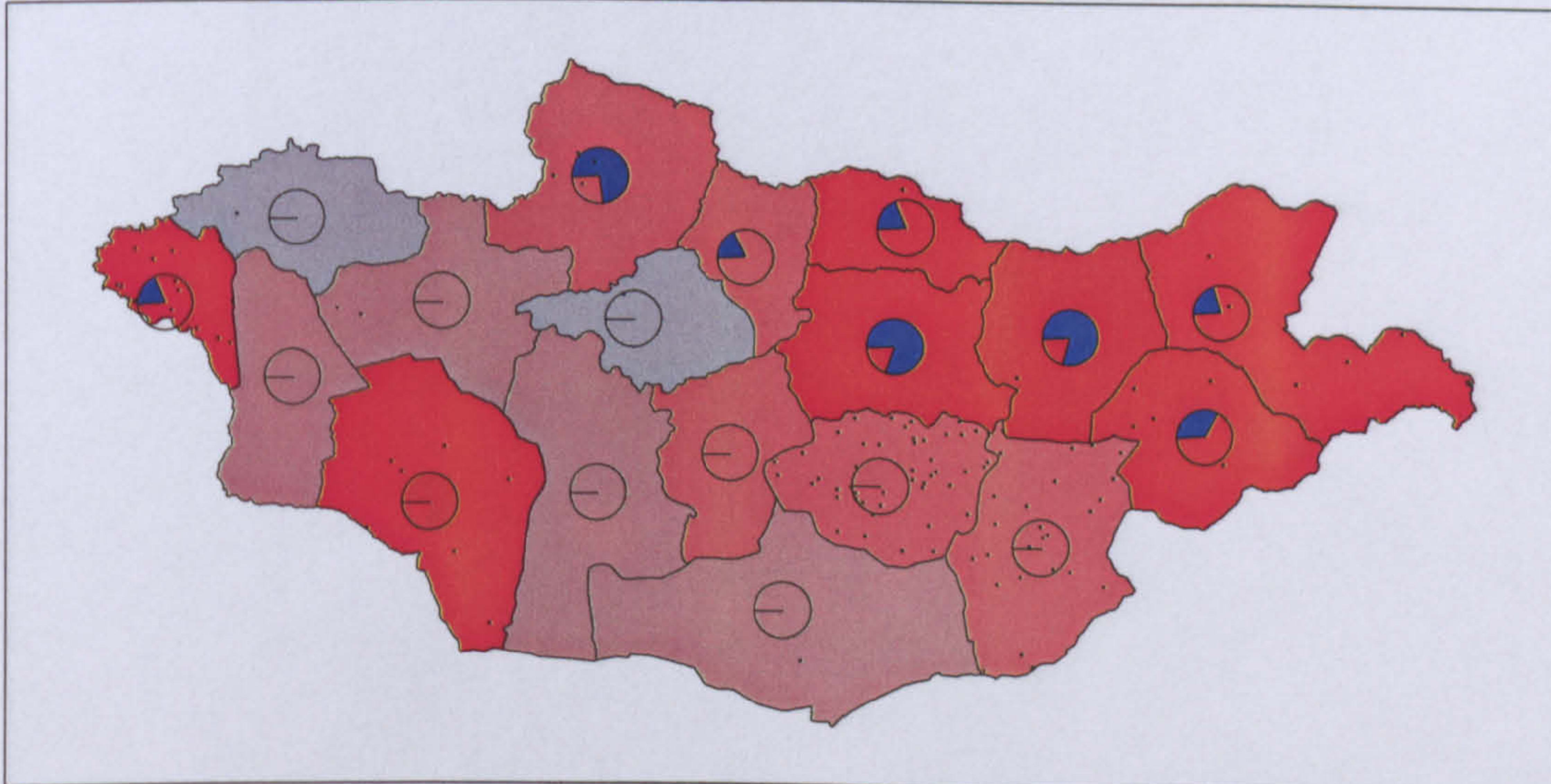
1975



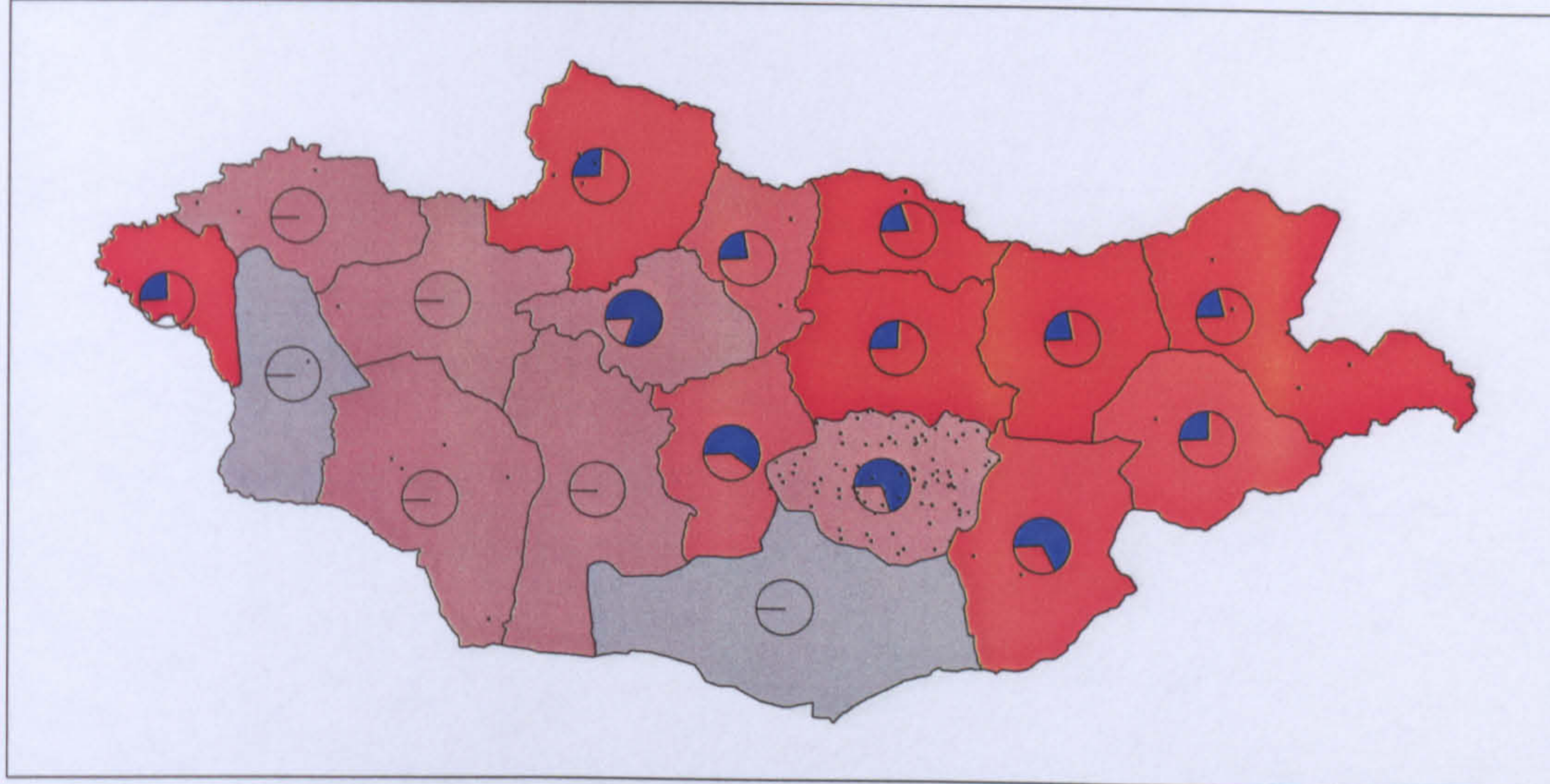
1976



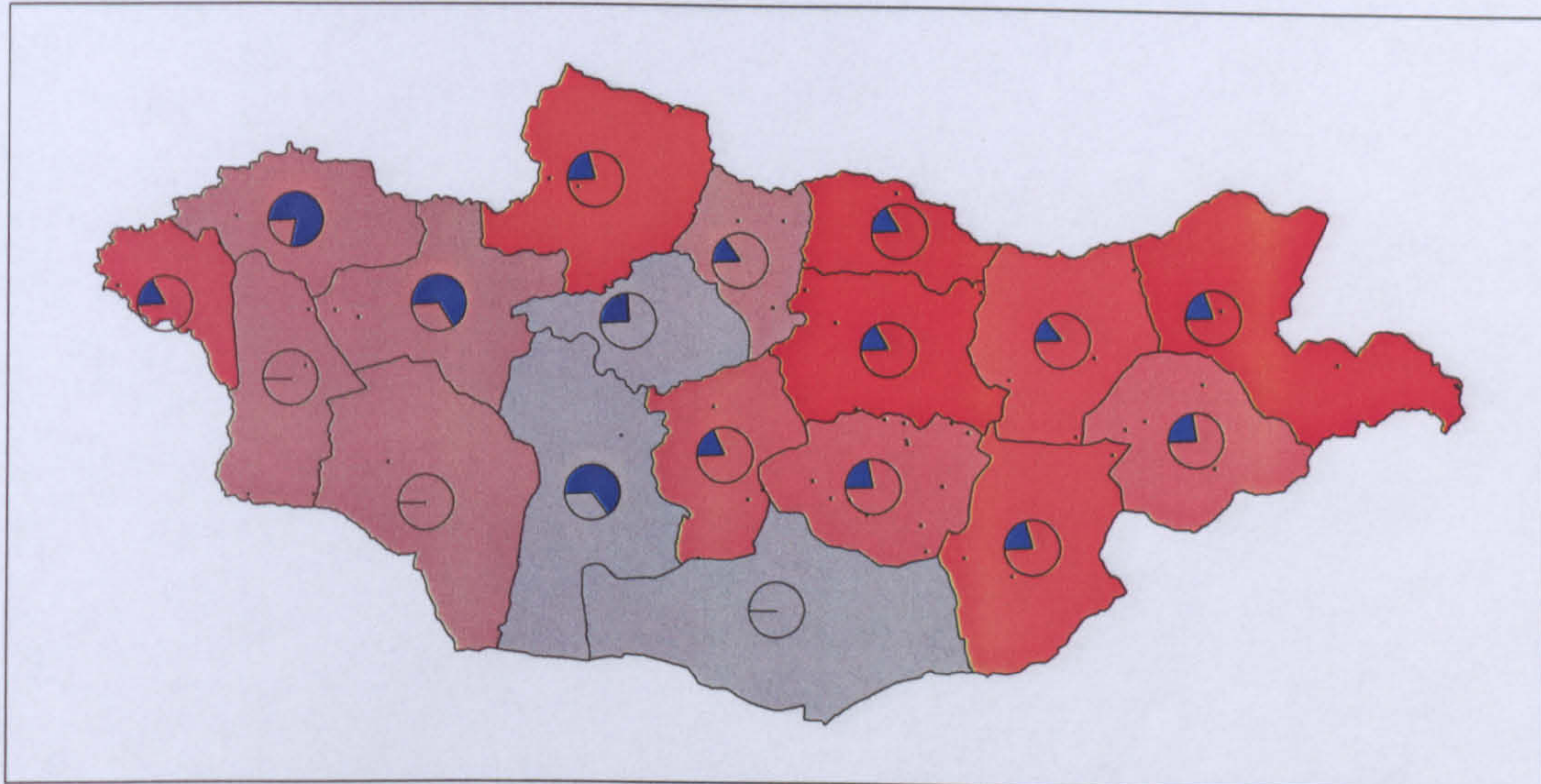
1977



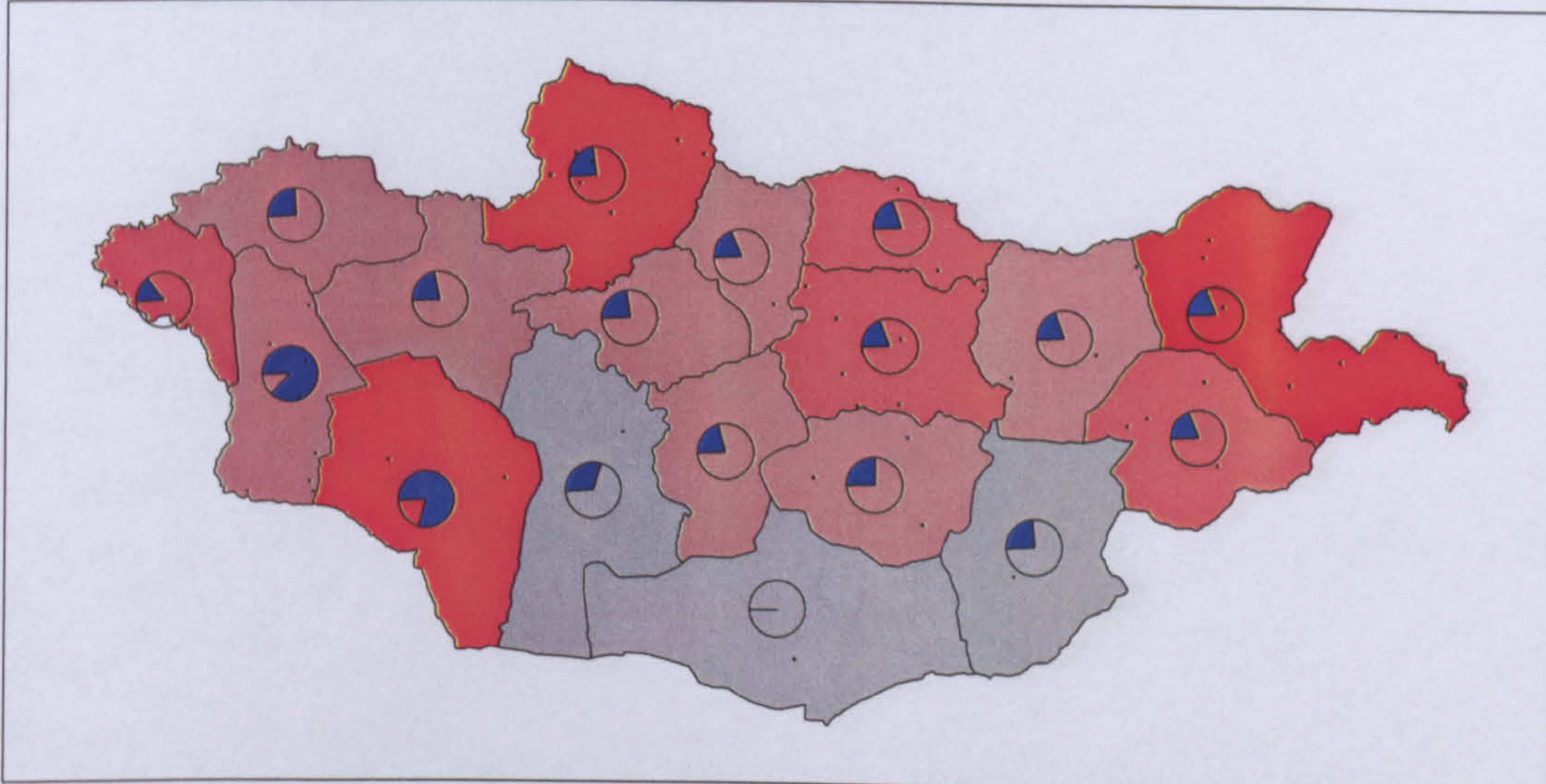
1978



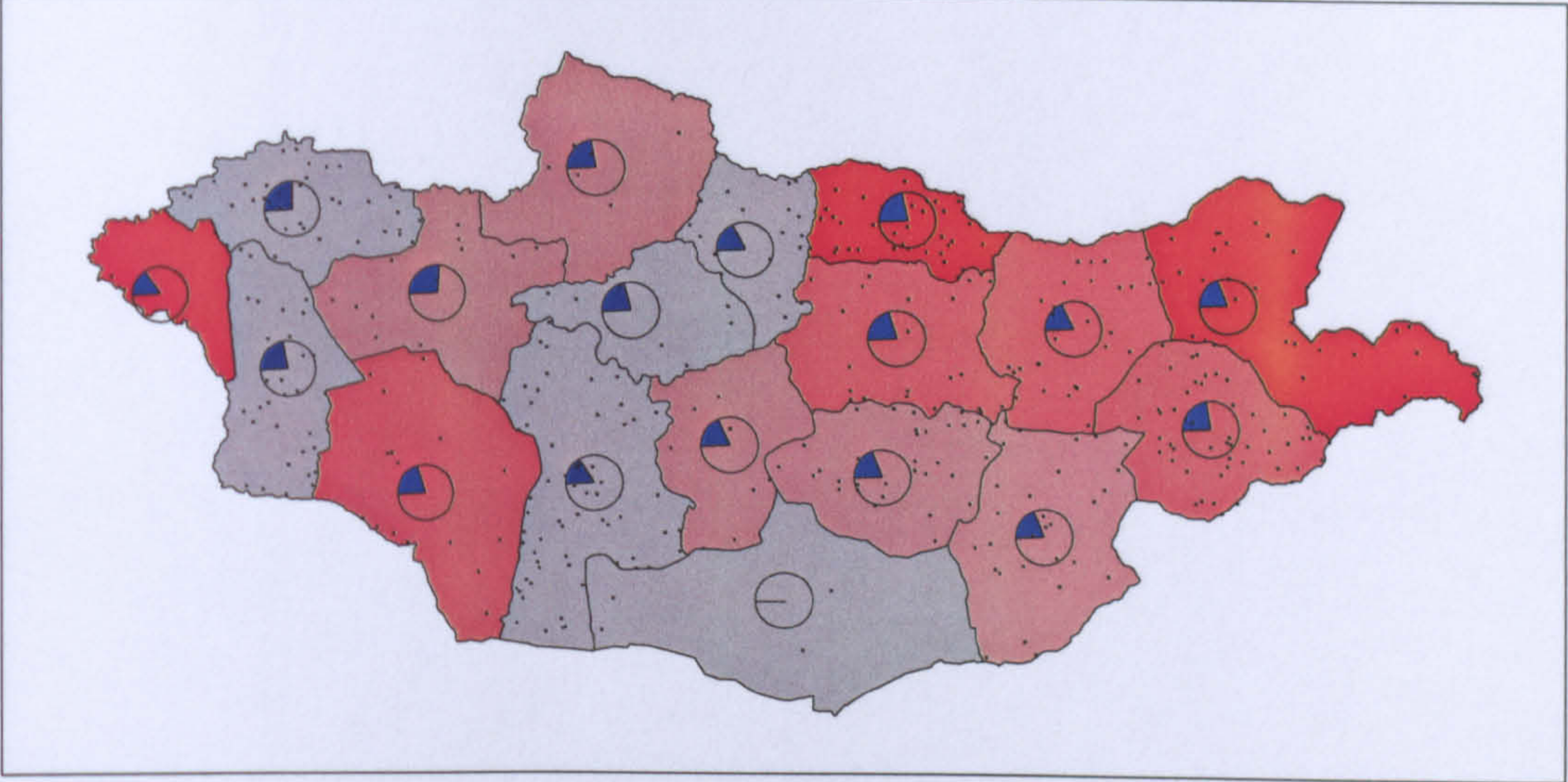
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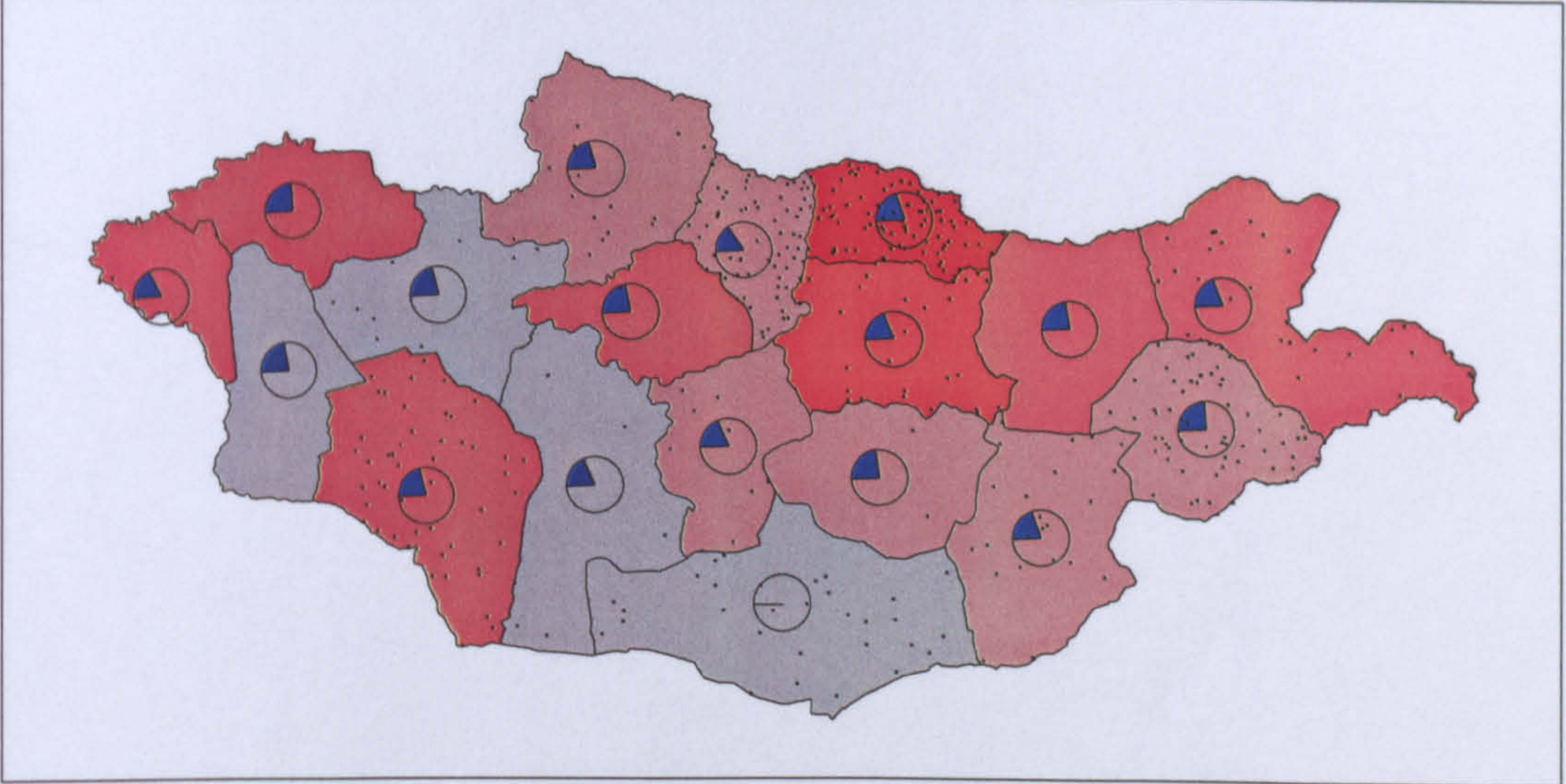
1980



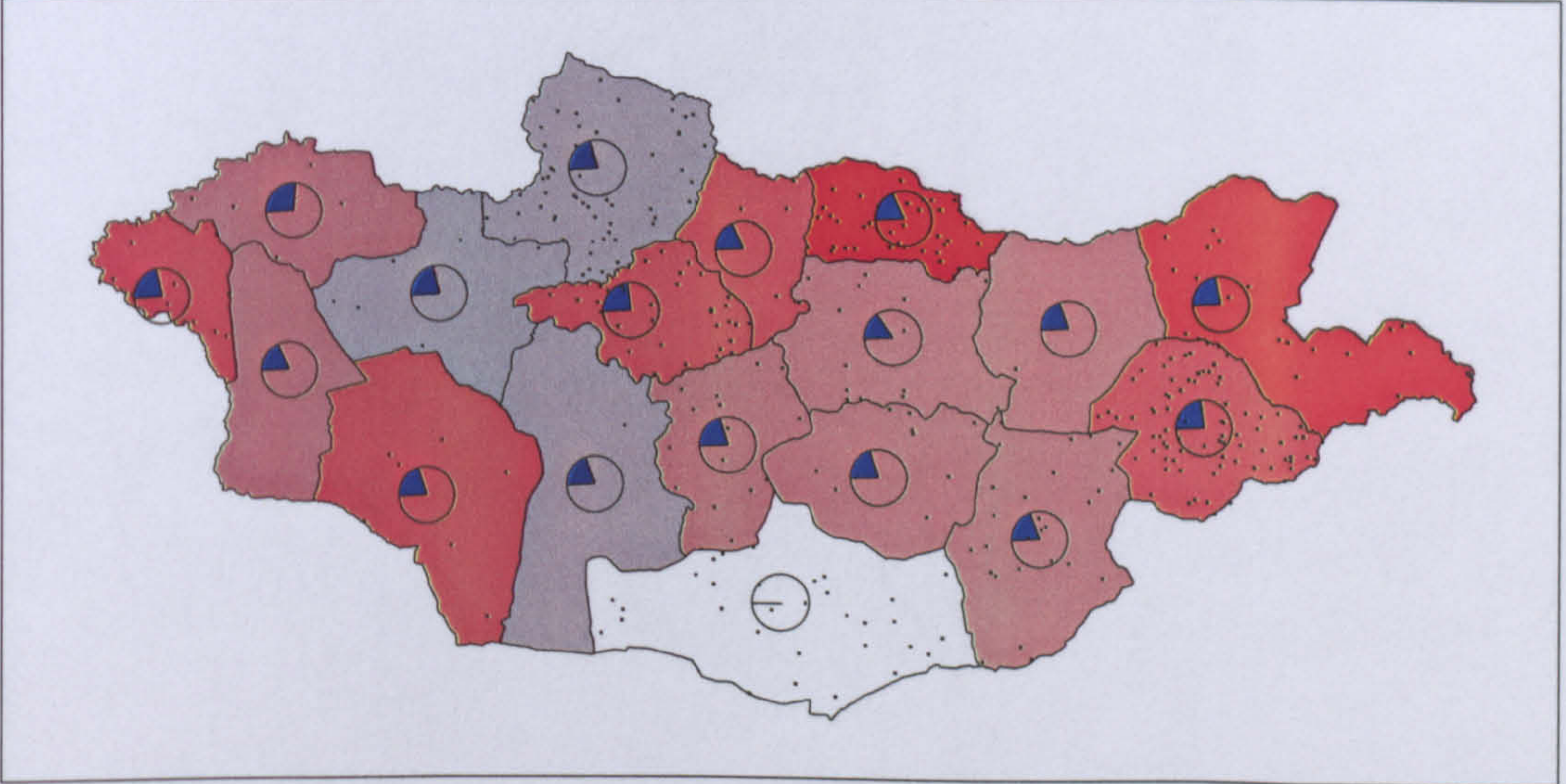
1981



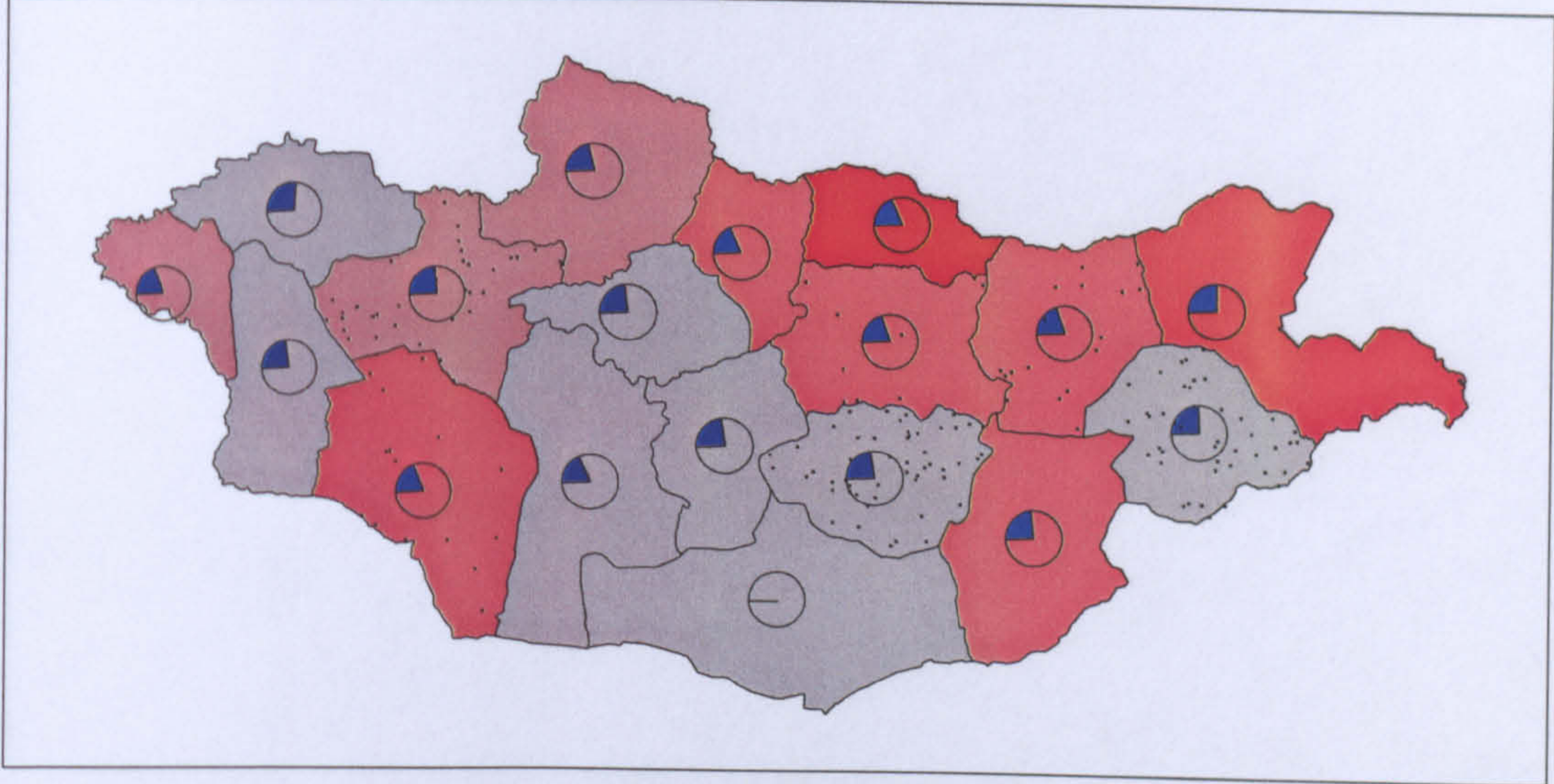
1982



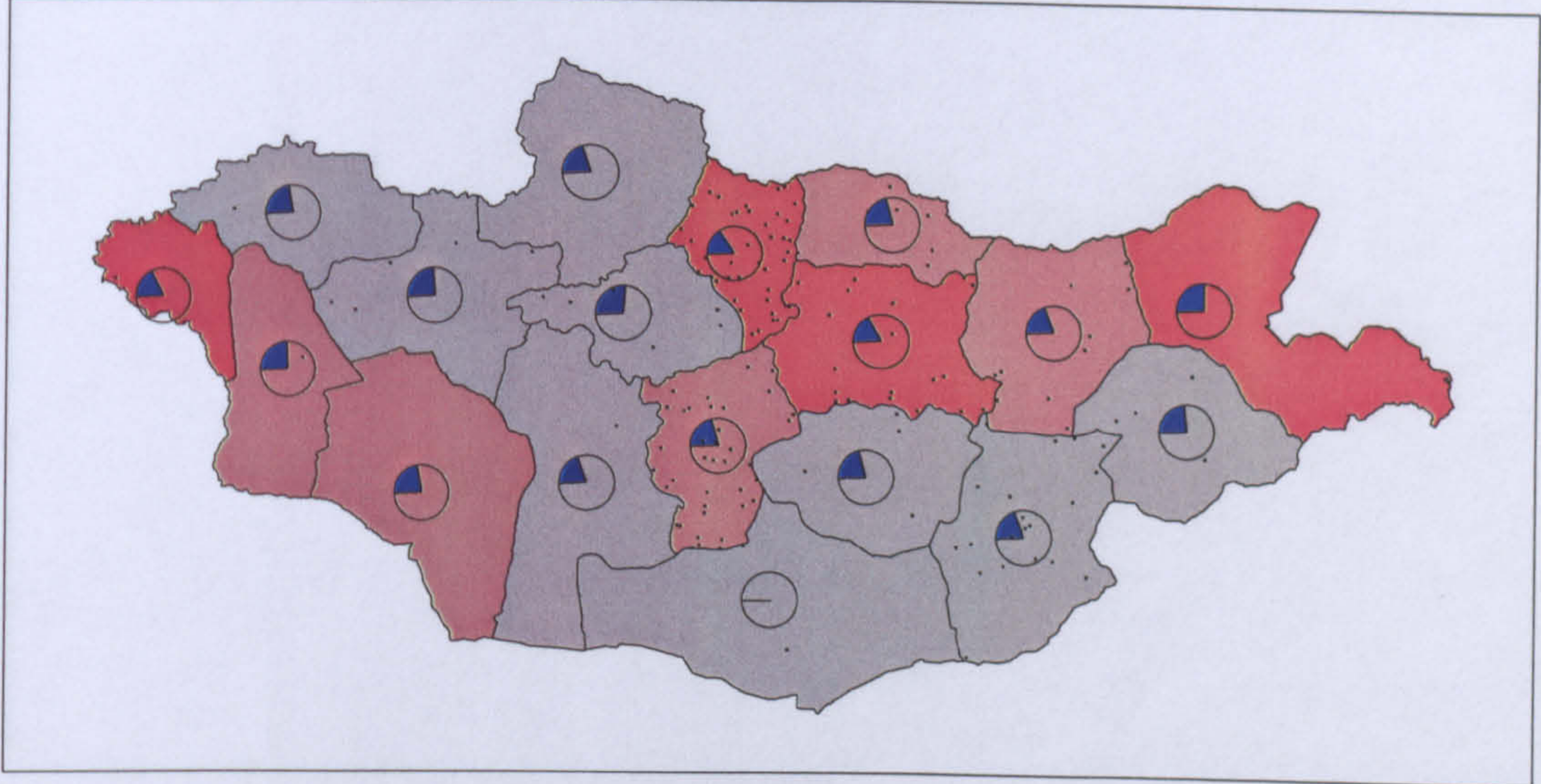
1983



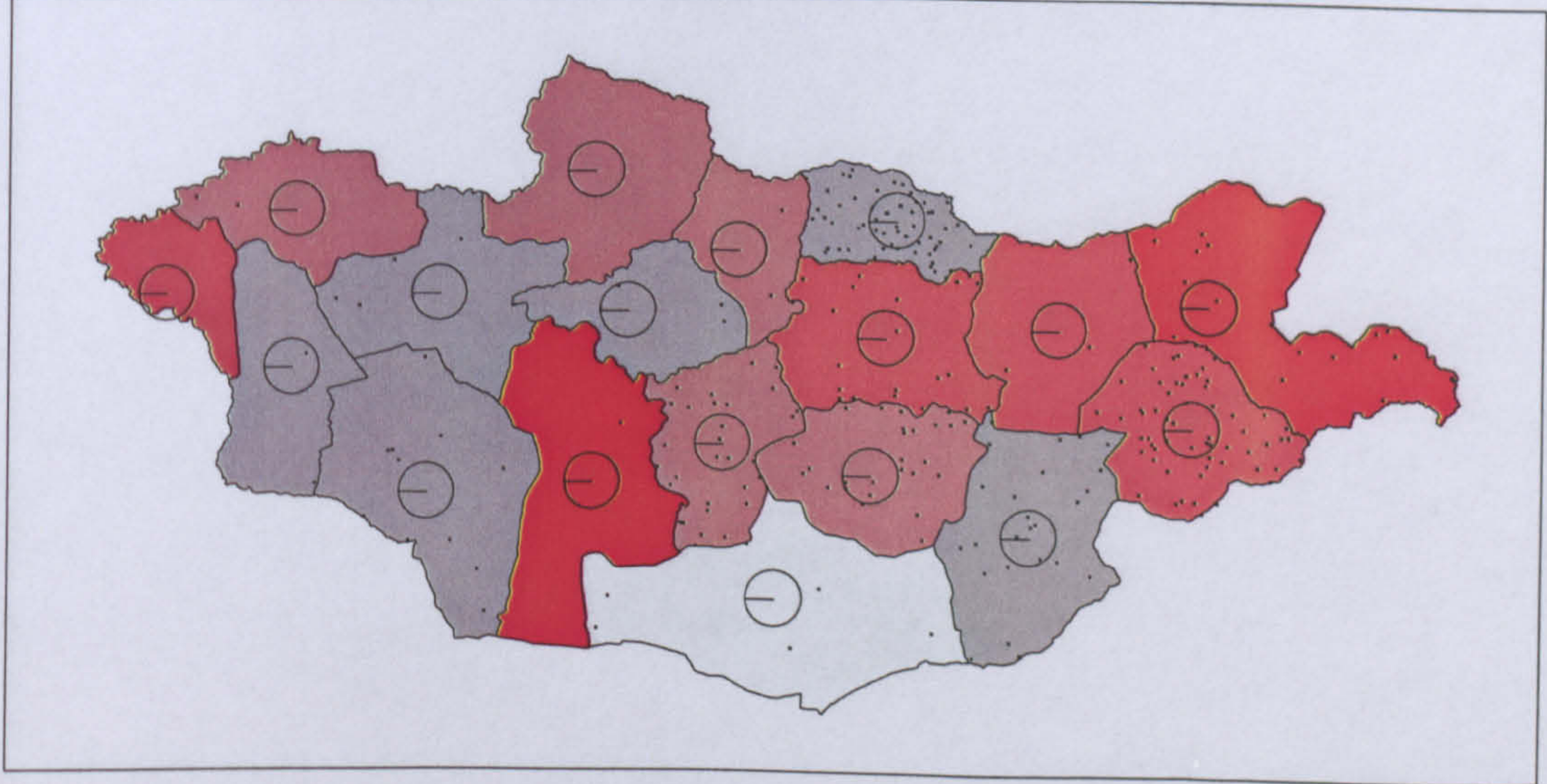
1984



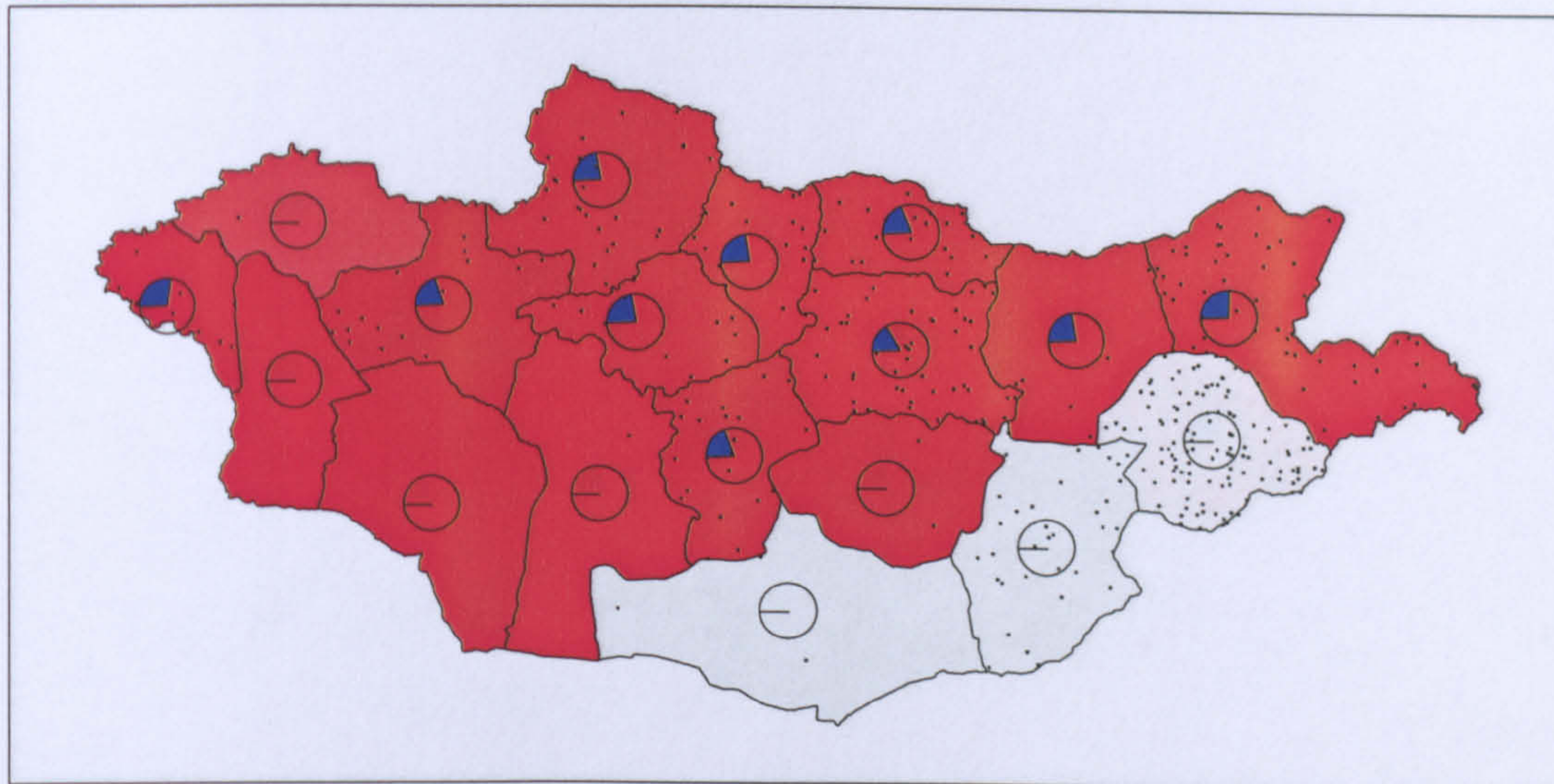
1985



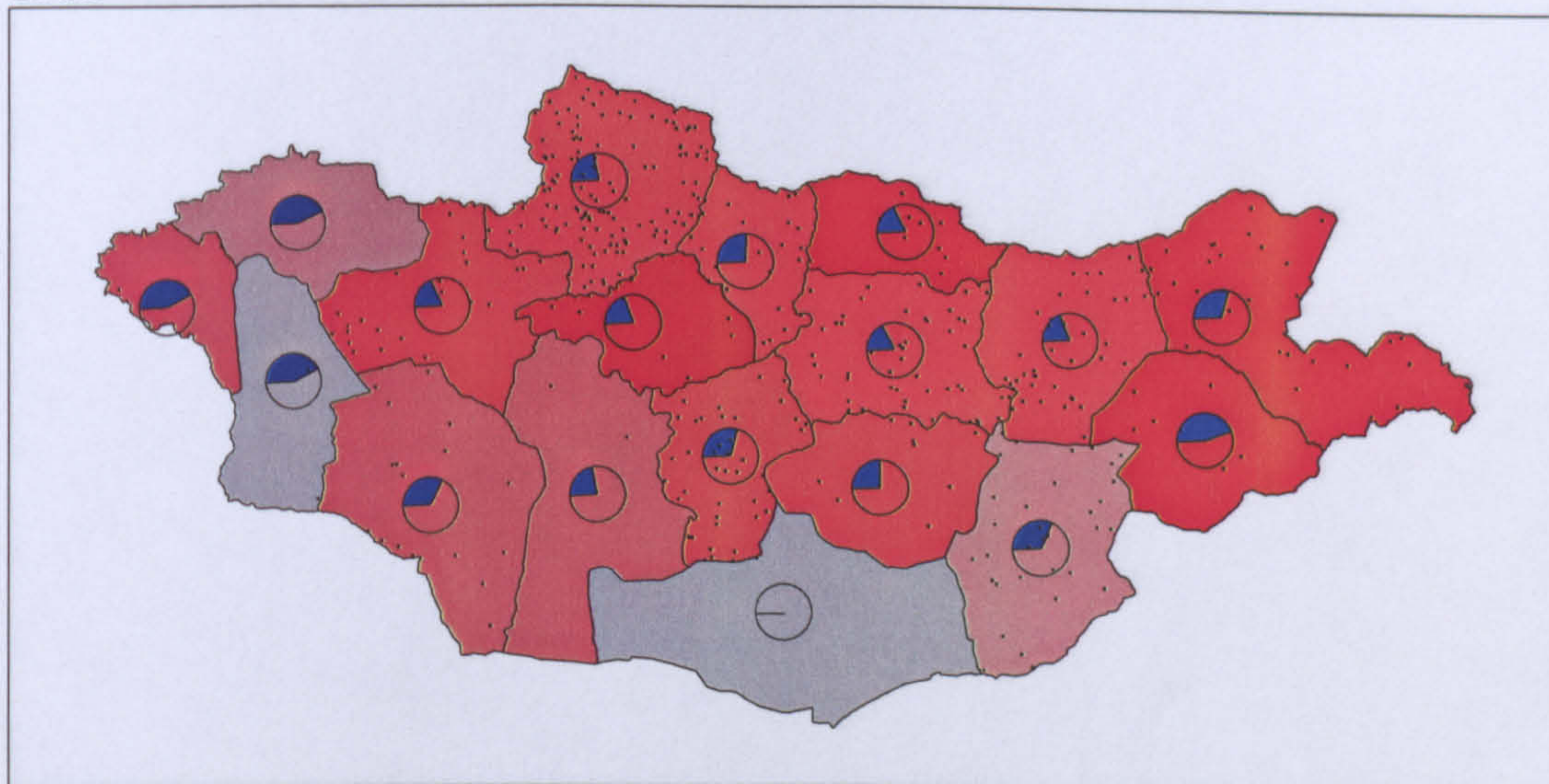
1986



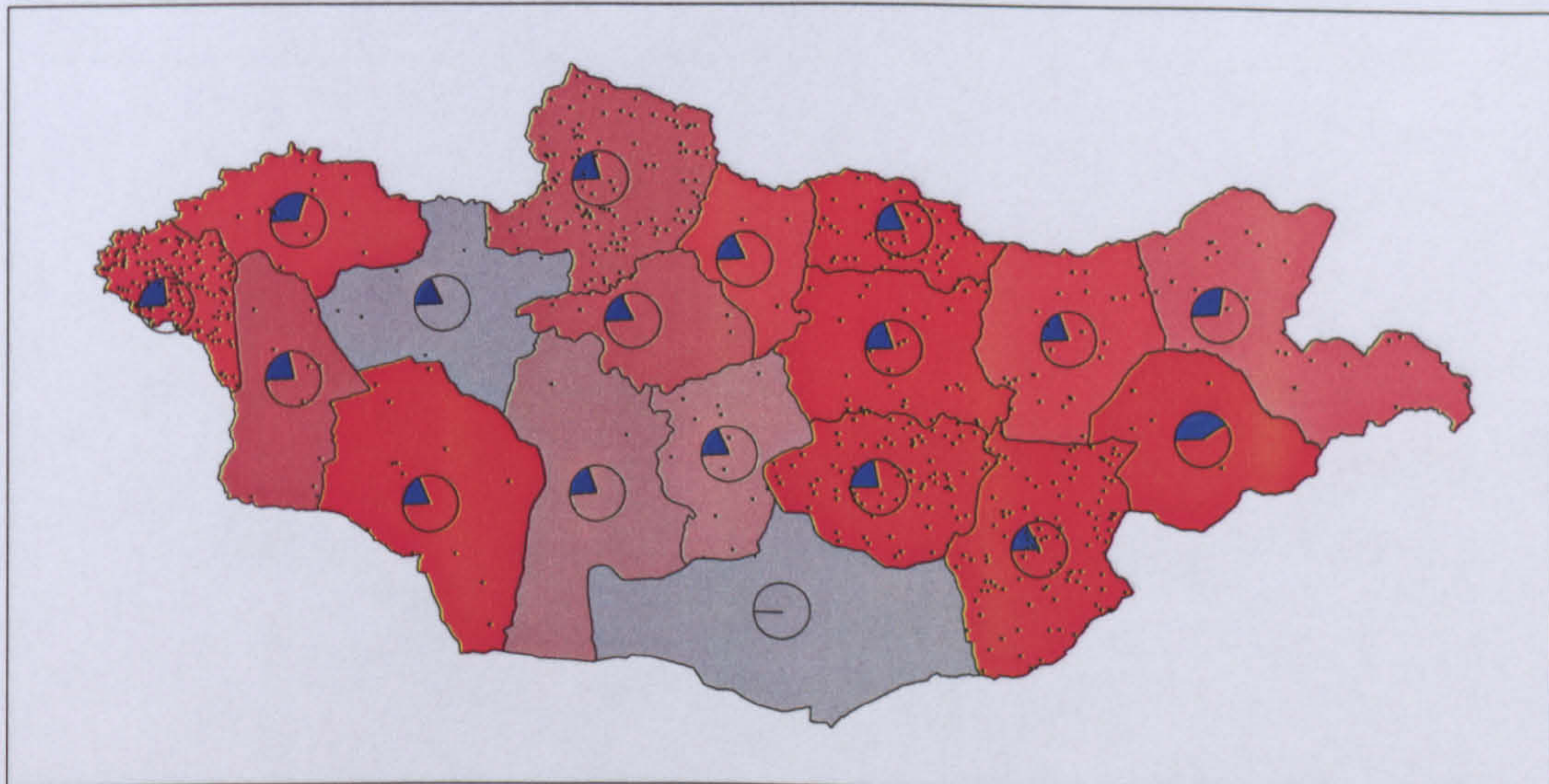
1987



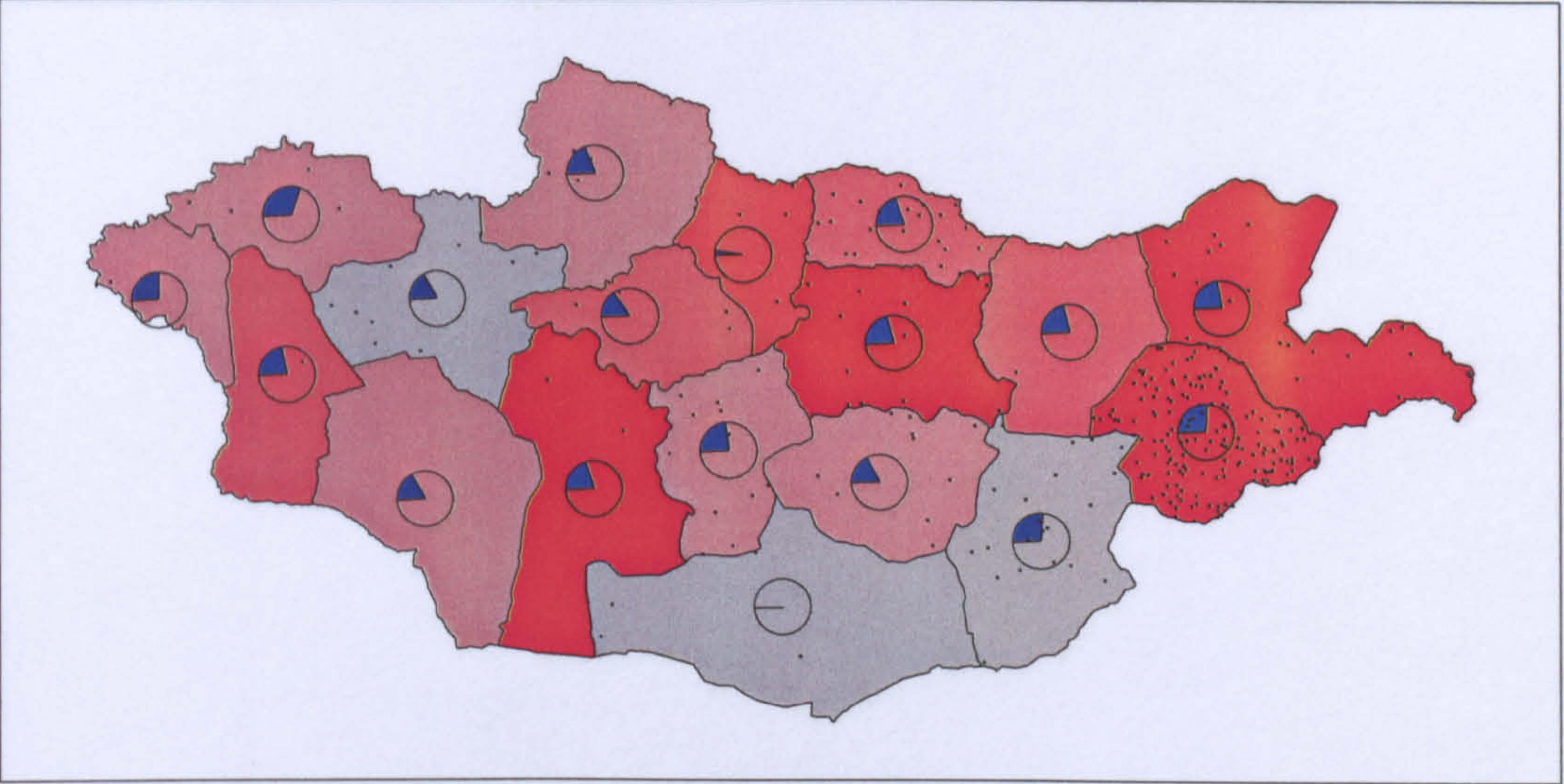
1988



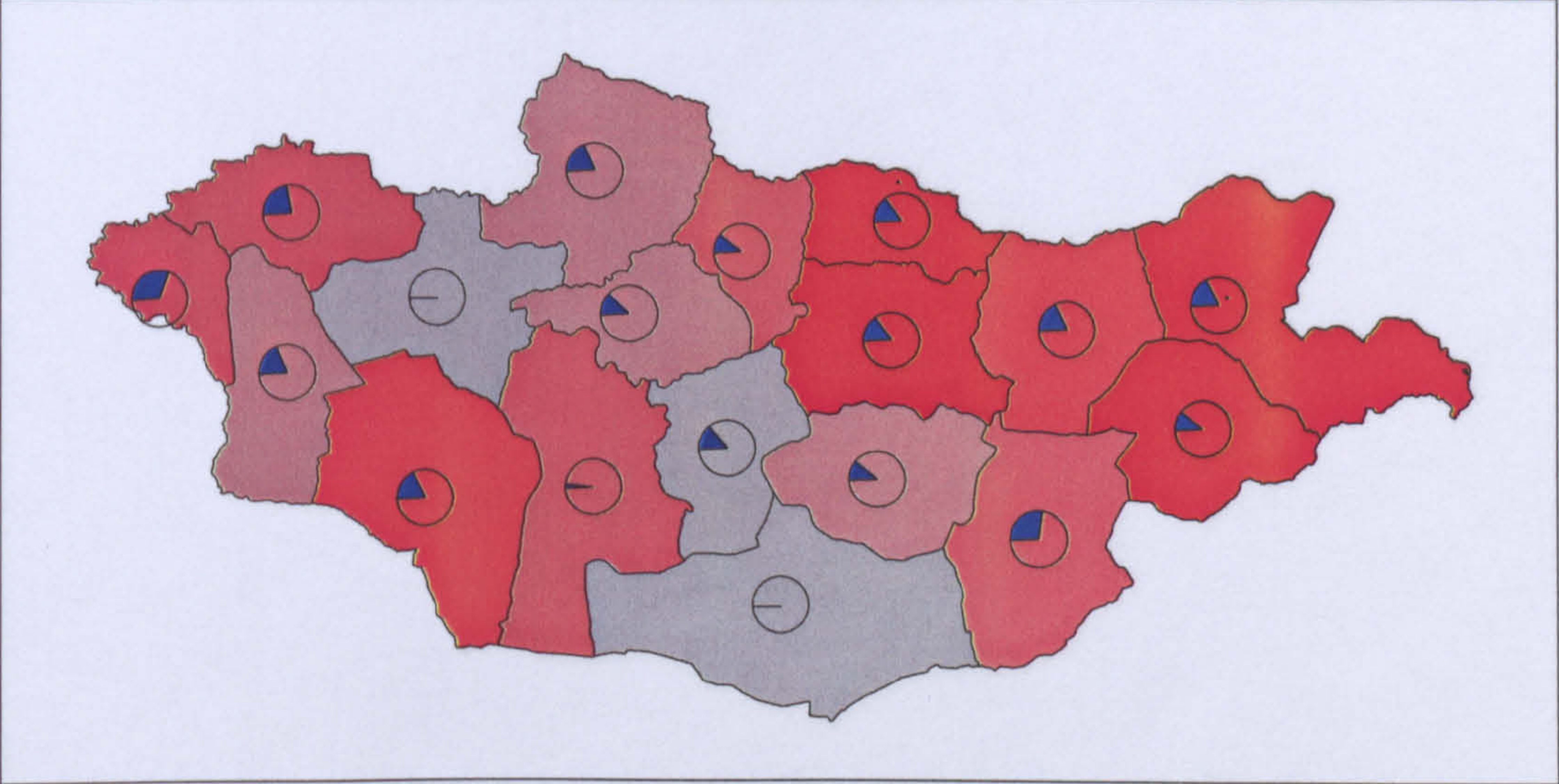
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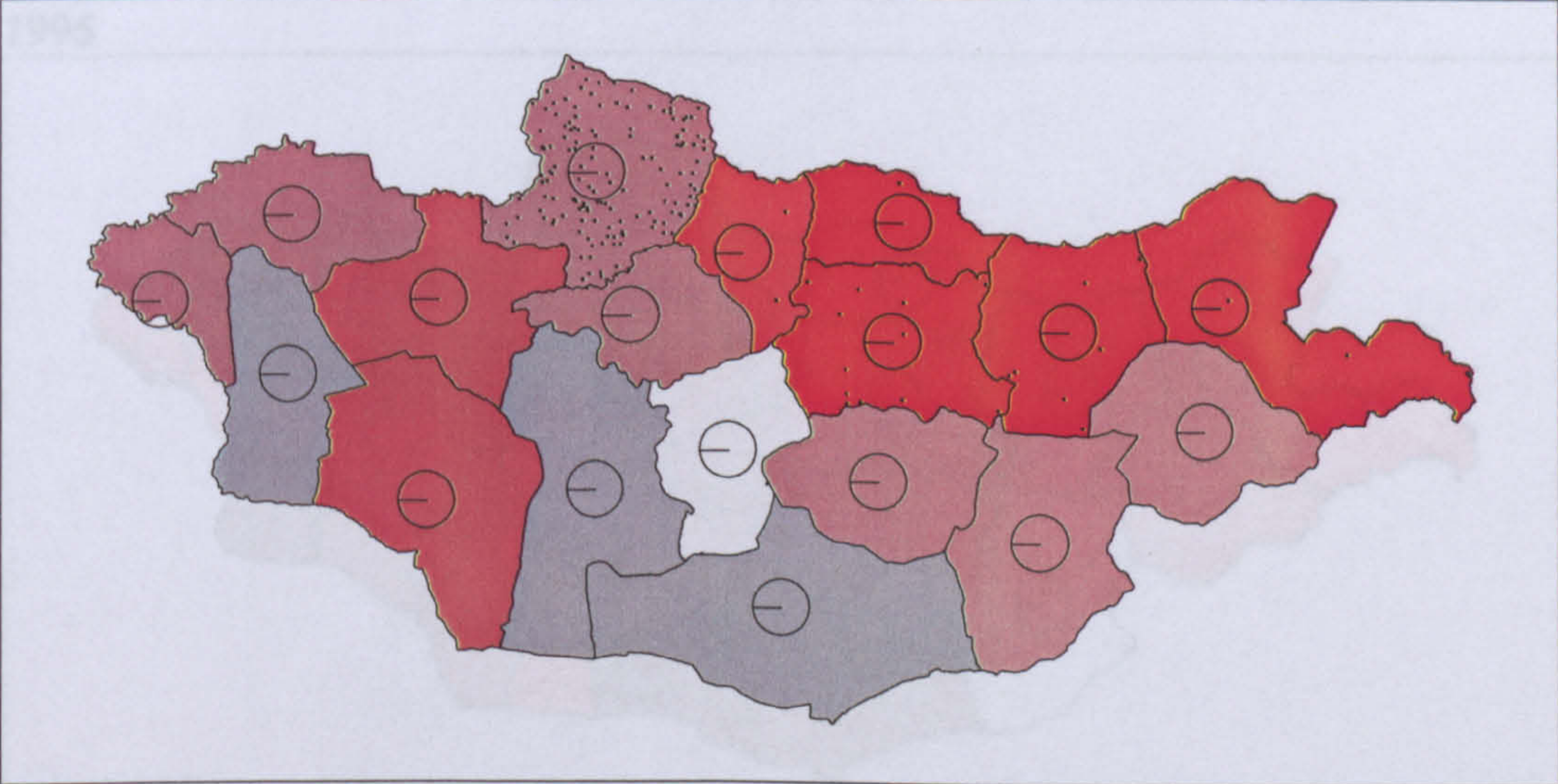
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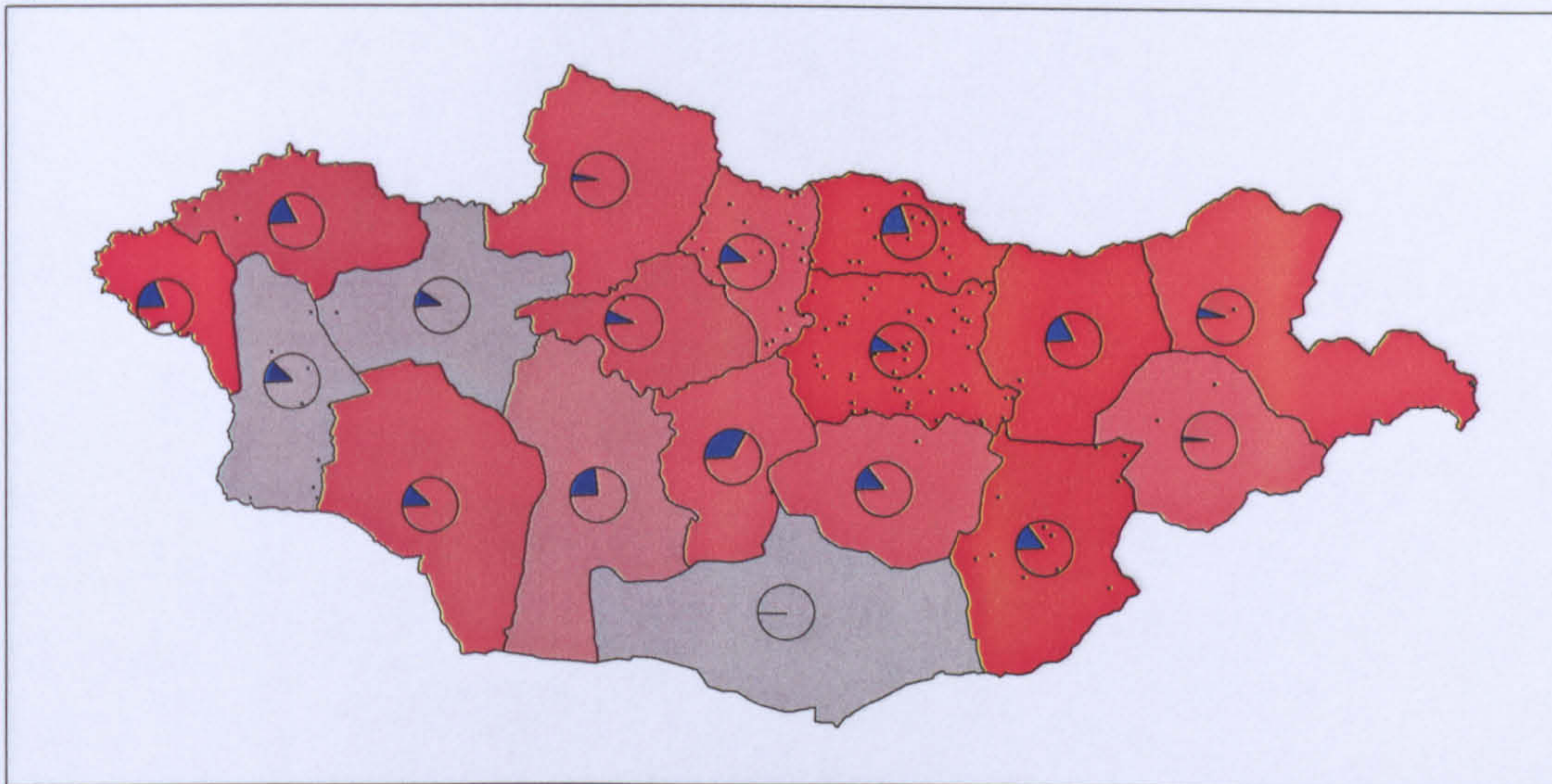
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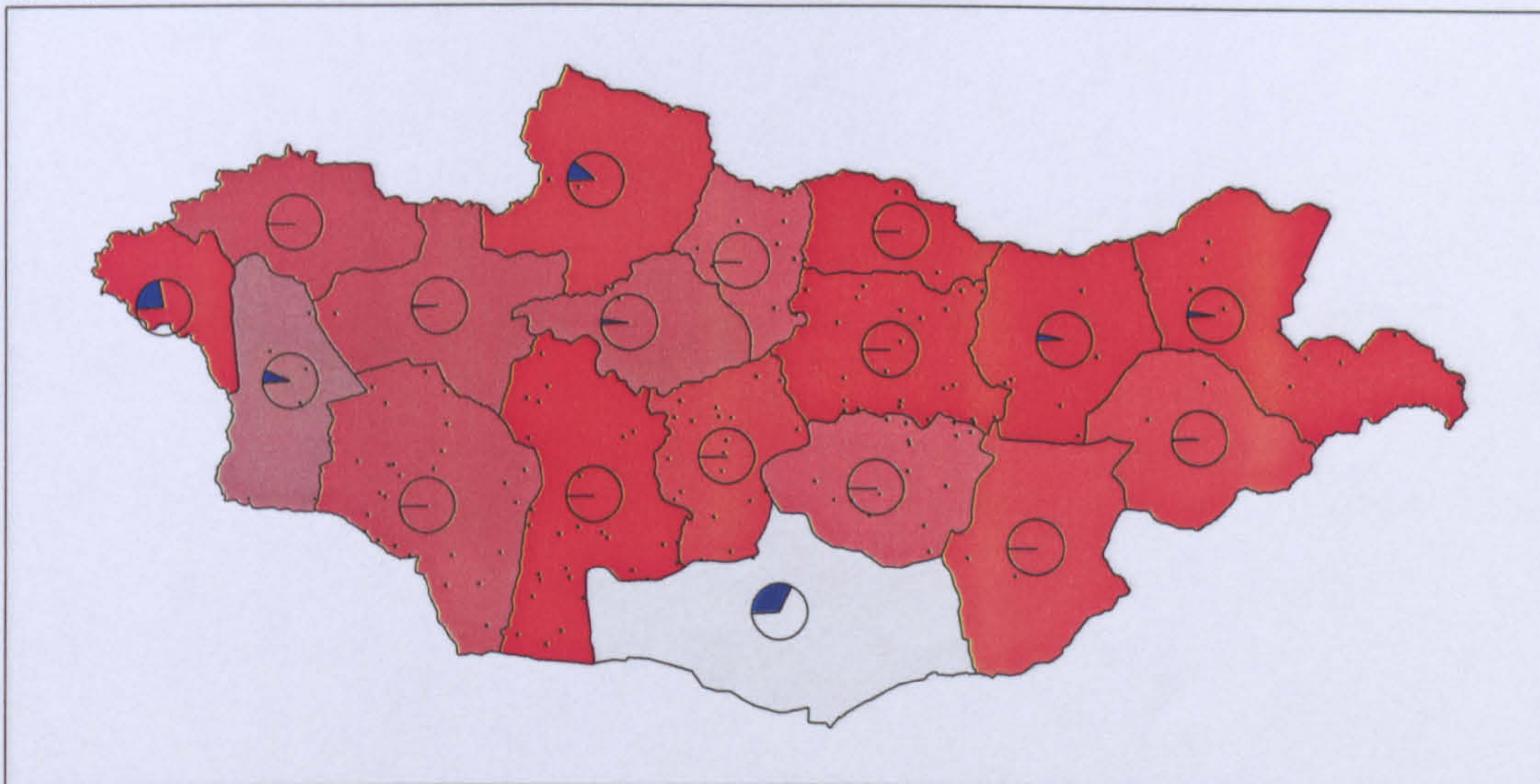
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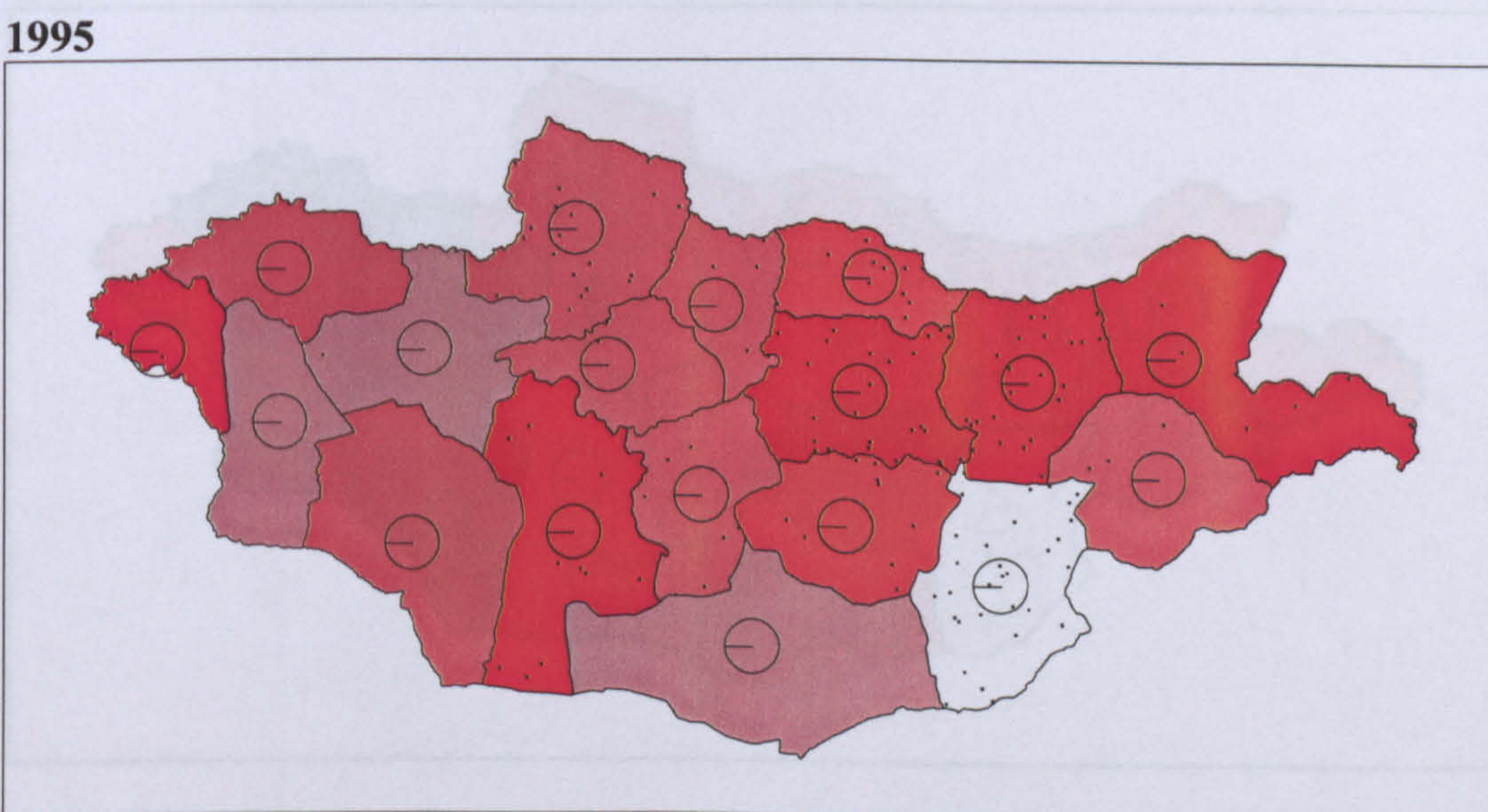
1993



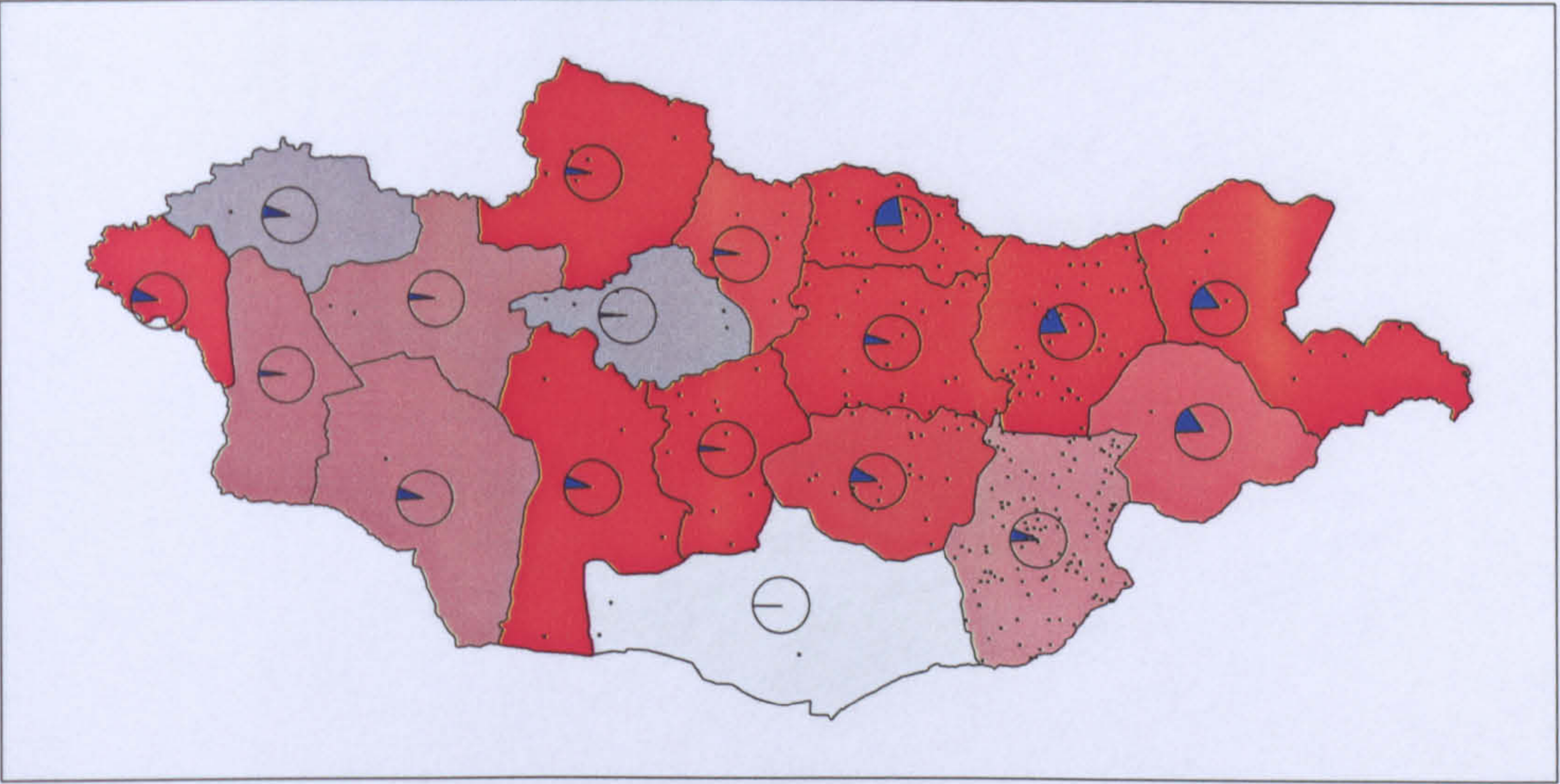
1994



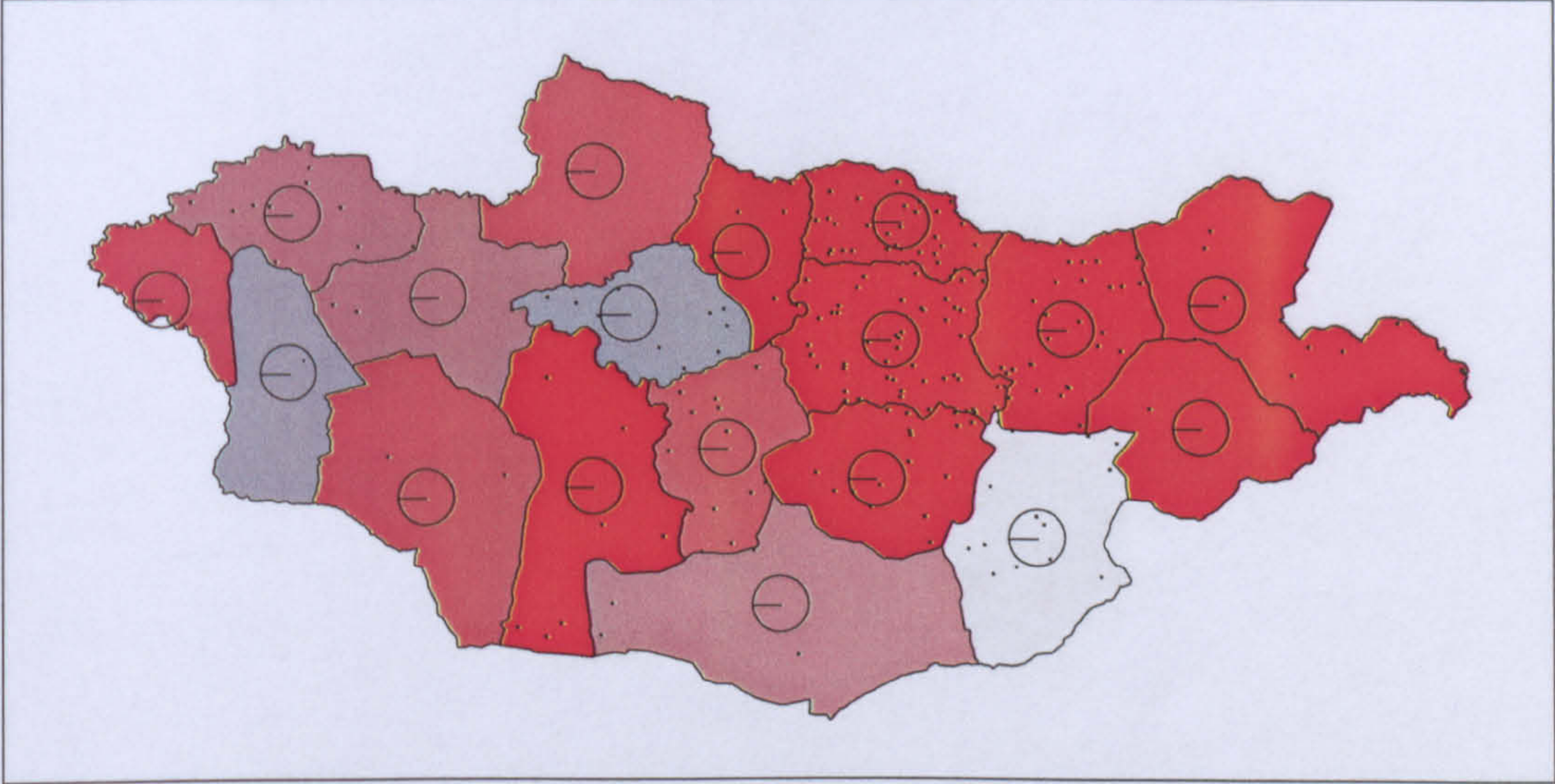
1995



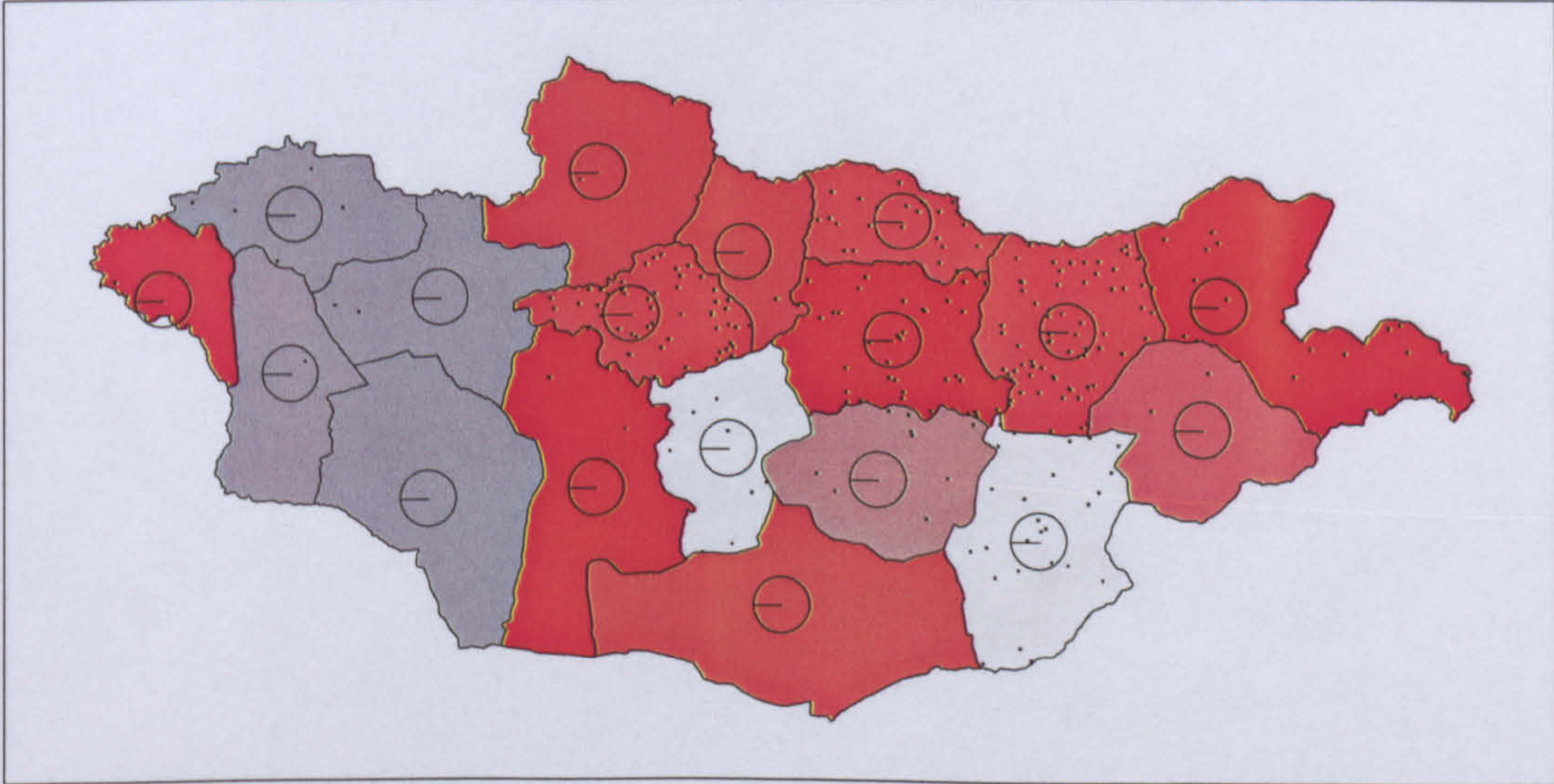
1996



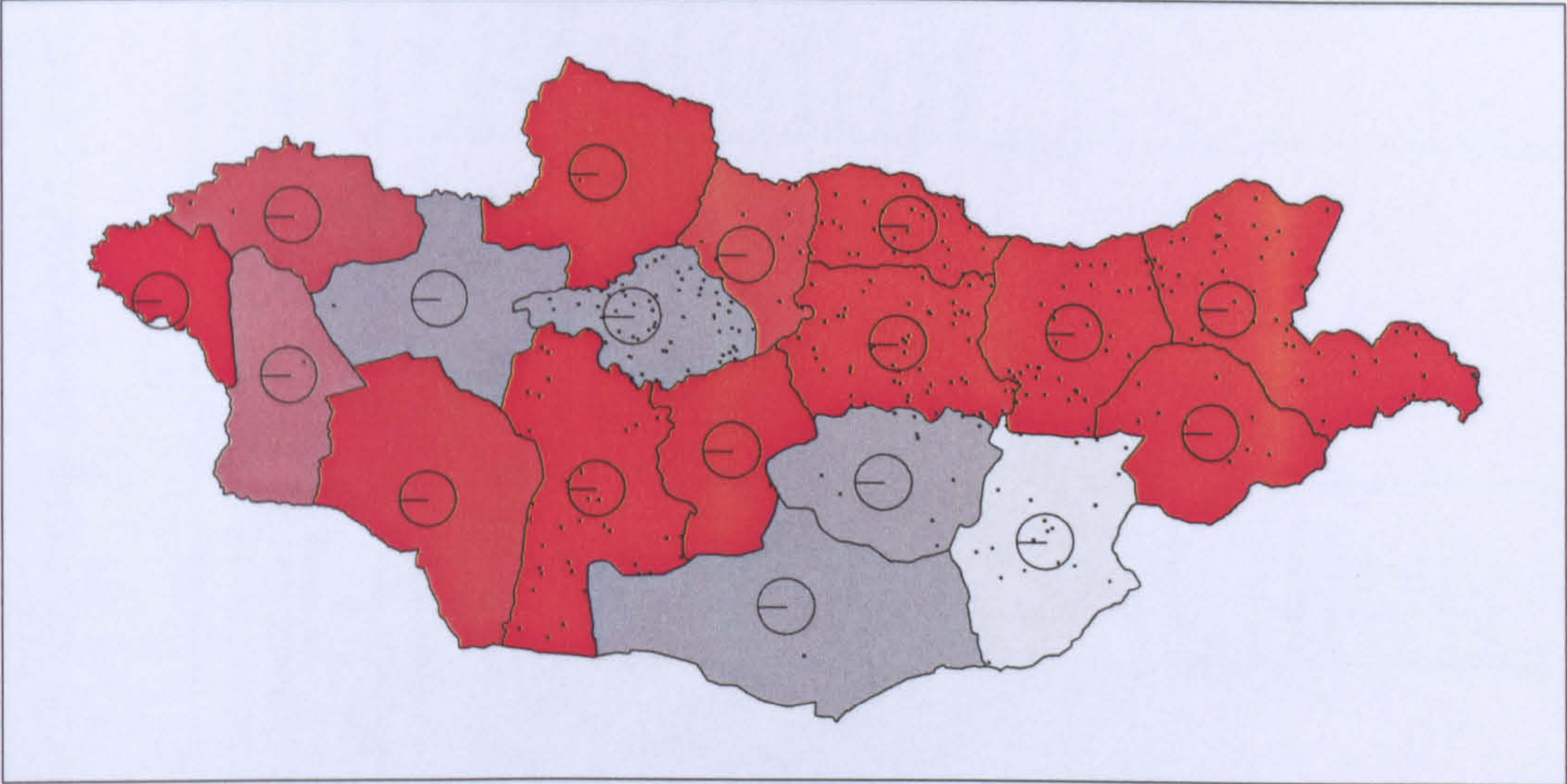
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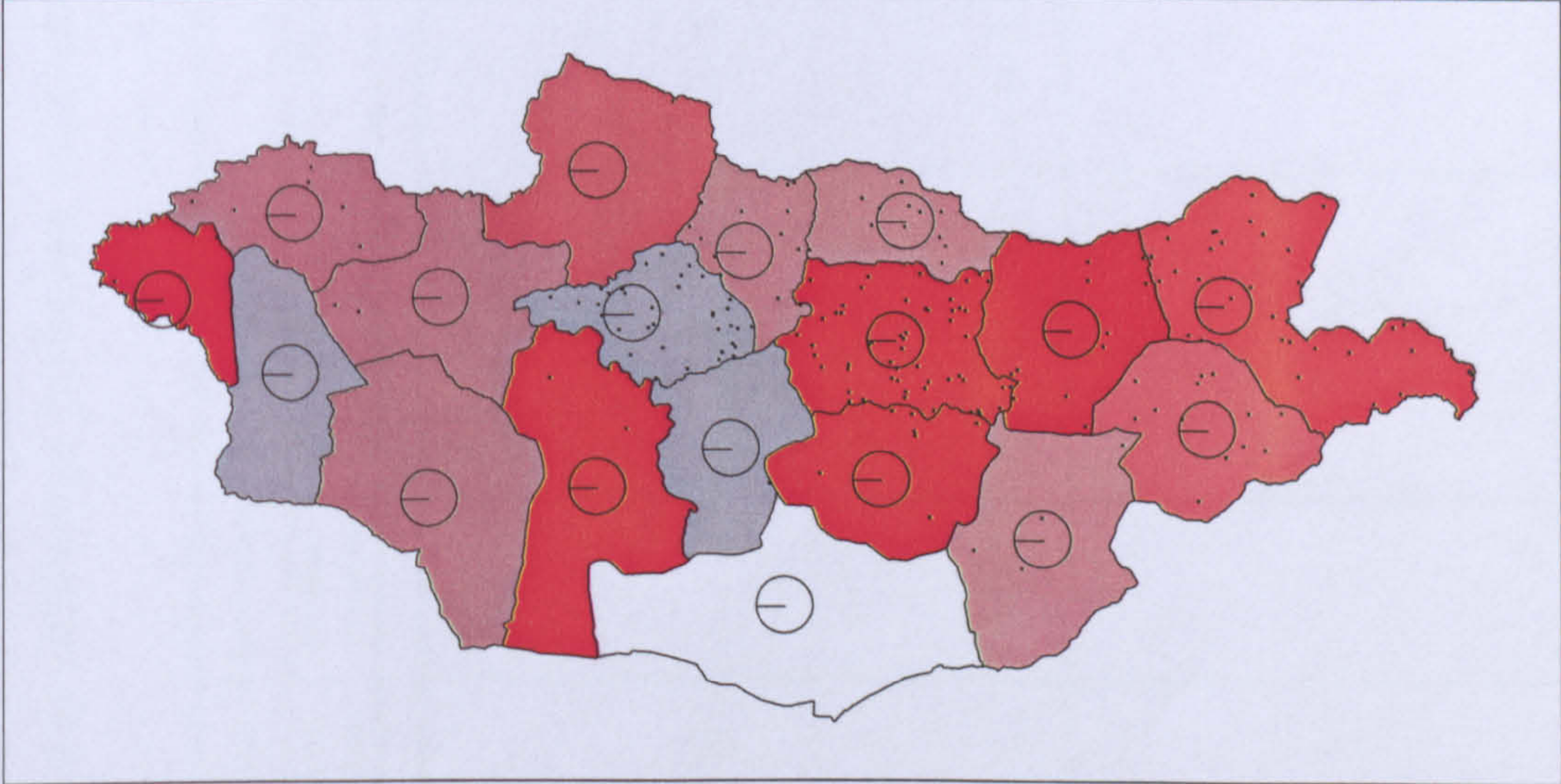
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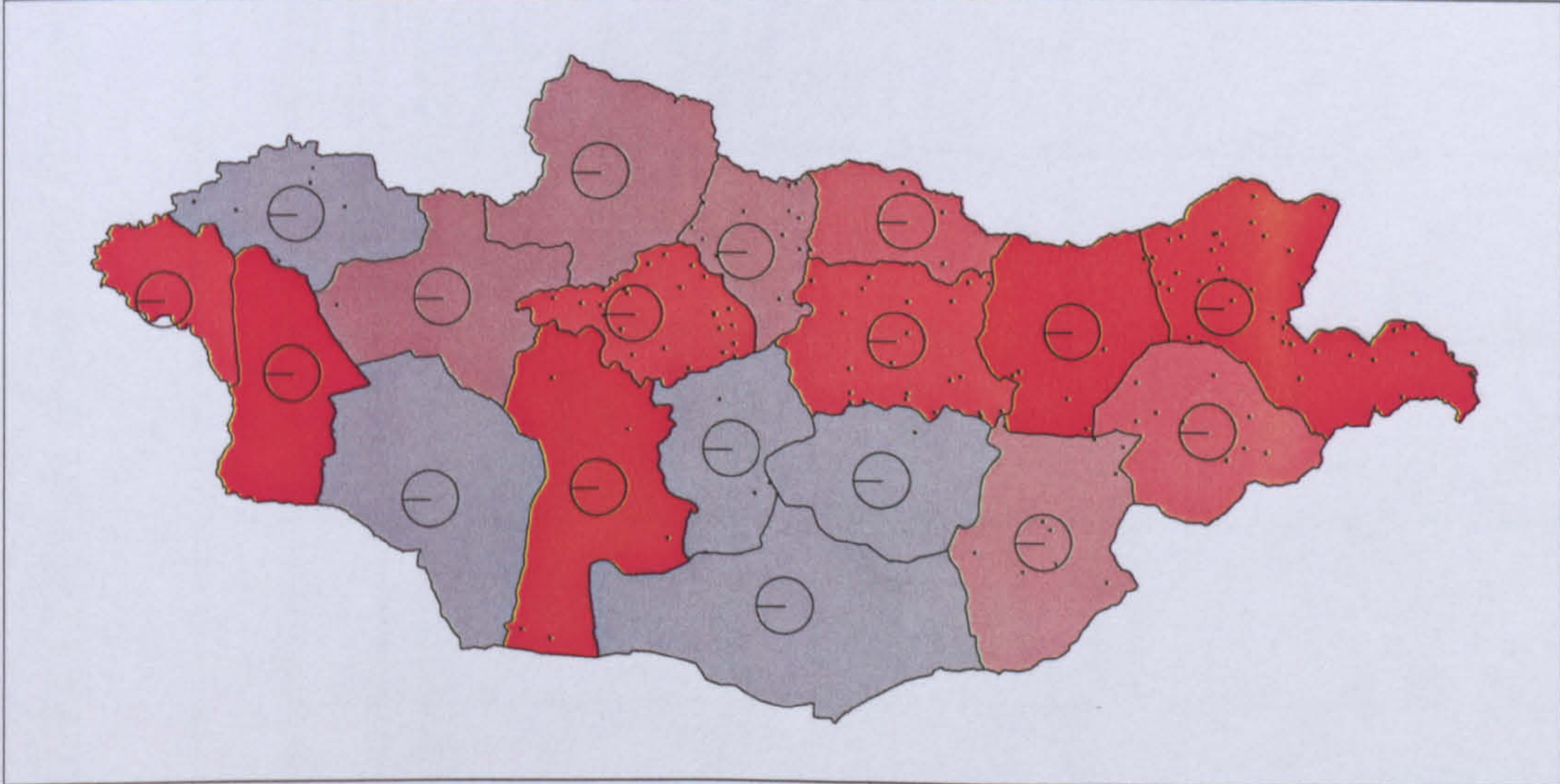
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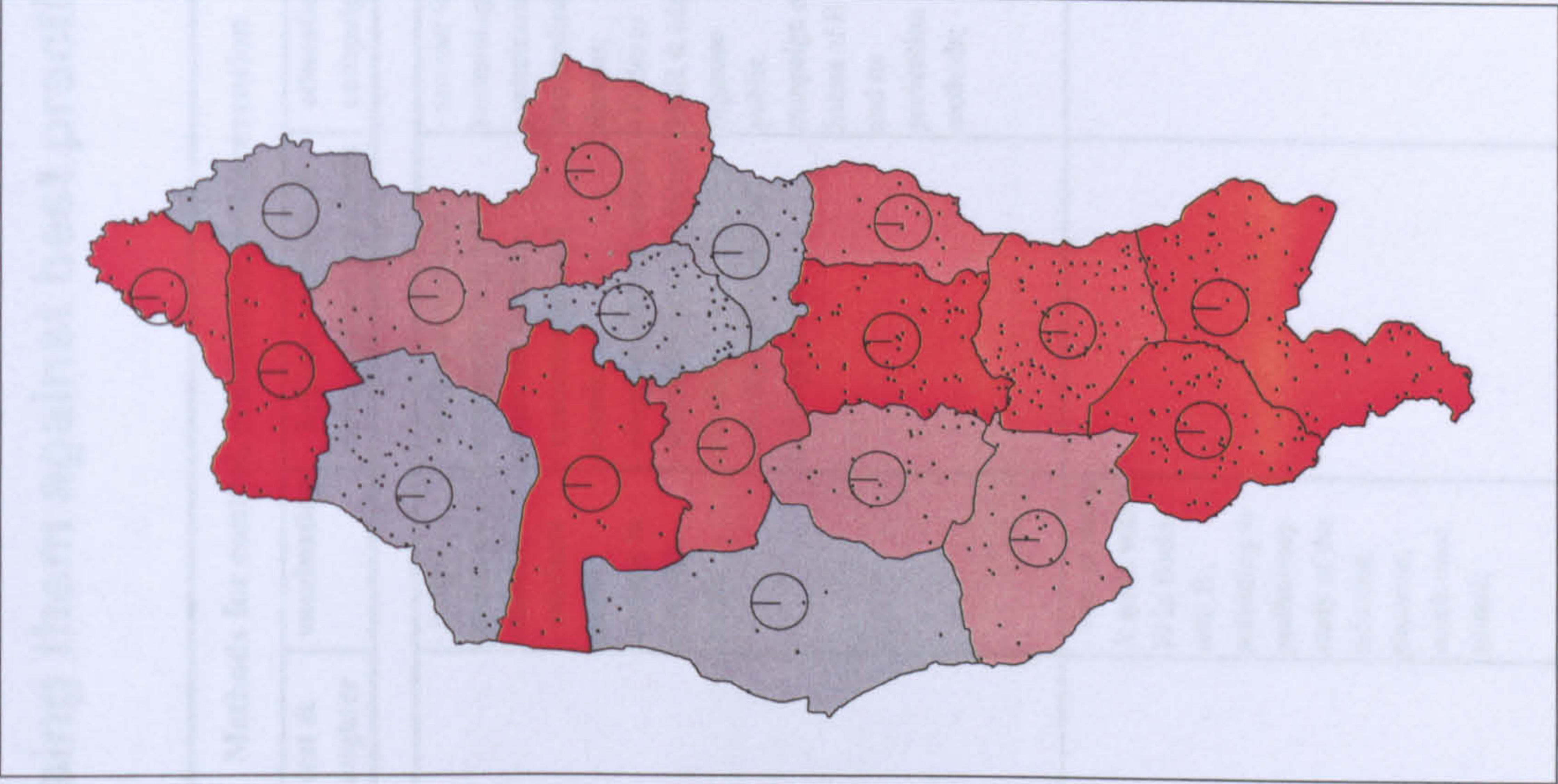
2000



2001



2002



Appendix 6.1.: Overview on the Mongolian surveillance policies and assessing them against best practice

Paper			Basic steps of Surveillance							Methods for control, eradication and prevention			
Term	year	Title	(i) objective	(ii) case definition	(iii) data collection	(iv) data analysis	(v) dissemination	(vi) implementation	(vii) evaluation	test & slaughter	vaccination	hygiene methods & management practices	education campaign
- Resolution of Ministers Cabinet Nr. 285 (<i>Molomjams et al, 1959</i>)	02.07.1959		- ordering measures in order to intensify the prevention activities against human and animal brucellosis;		- investigate geographical risk areas; - initiate production of lab tests; - establish department of testing in Aimag;						- initiate production of vaccines; - vaccinate people working in high risk farms;	- implement treatment measures for infected people and animals; - quarantine infected animals; - slaughter infected animals; - establish herds of infected animals; - develop regulations to exchange animals;	- seminar for bacteriologists, veterinarians and medical doctors; - Order to MoH & MoA: organise public campaign on harms of B and its prevention methods;
- Order of MoA Nr. 287 (<i>Ministry of Agriculture, 1959</i>)	May 1959	Guideline on the use of S-19									- Vac. of sheep & goats with S-19 in flocks with B-, according to preliminary study of the infection situation; -mark vacc. animal;		

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Term	year	Title	(i) objective	(ii) case definition	(iii) data collection	(iv) data analysis	(v) dissemination	(vi) implementation	(vii) evaluation	test & slaughter	vaccination	hygiene methods & management practices	education campaign
- Resolution of the Minister's Cabinet Nr. 52, mentioned in <i>(Enkhbaatar L et al. 2004)</i> , do not have original	14.02.1963	- strengthening of Health Services (epidemiology).	- implement project Mongolia 0001		- epidem. Study on b in 1965 - 66 - B serological survey in human in 1967 - 68								
- Order of MoA Nr. 339 <i>(Ministry of Agriculture, 1964)</i>	22.07.1964	Performance of tests for B in animals of some Aimag	- eliminate B & implement resolution Nr. 285	- supply methodological advice for tests by scientist;	- perform B tests in some Aimag;		- scientists discuss results of tests with MoA;	- sending manpower to the concerned Aimags; - provide office space & transport;		- implement measures to quarantine and slaughter infected animals;	- vacc. sheep, goats & cattle with S-19;	- mark & isolate infected animals; - test male animals used for mating;	

Paper			Basic steps of Surveillance							Methods for control, eradication and prevention			
Term	year	Title	(i) objective	(ii) case definition	(iii) data collection	(iv) data analysis	(v) dissemination	(vi) implementation	(vii) evaluation	test & slaughter	vaccination	hygiene methods & management practices	education campaign
- Resolution of MPRP Central Committee and Minister's Cabinet Nr. 189/216 (Tsedenbal, 1965)	16.06.1965	measures to fight animal glanders, brucellosis and tuberculosis (bilateral assistance of COMECON States)	- improve the prevention and fight against glanders, brucellosis and tuberculosis; - goal of eliminating animal glanders, brucellosis and tuberculosis within 1970;		- test for animal glanders, brucellosis and tuberculosis;			- establish a Gov. Committee to organise the measures and supply the preparatory materials to fight animal glanders, brucellosis and tuberculosis (managerial structure, manpower, testing material); - establish local Committee to prevent these diseases in animals; - provide funding; - organise course for 230 lab workers; - implement survey and tests; - establish a State Veterinary & Sanitary Laboratory in order to fight infection in human & animal; - establish laboratories in Aimags; - provide ear tags; - allocate funds for the therapy of people infected in outpatient facilities;	- discuss the progress of prevention activities in meetings with local agricultural unions, farms, groups, party committees and gov.;	- slaughter positive tested animals, and use them for economic consumption under the monitoring of the Veterinary offices;	- vaccinate healthy people working with infected animals;	- quarantine infected animals; - isolate infect. animals in special herds;	- organise public advocacy on the harm of B, the measures to fight B. and prevention; - implement guidelines to prevent brucellosis in herders in contact with infected animals;
- Order of MoH Nr. E-434 (Ministry of Health, 1966)	07.01.1966	Guidelines to prevent human B	- to implement Resolution Nr. 189/216;								-vaccine therapy for people with chronic B.;		

Paper			Basic steps of Surveillance							Methods for control, eradication and prevention			
Term	year	Title	(i) objective	(ii) case definition	(iii) data collection	(iv) data analysis	(v) dissemination	(vi) implementation	(vii) evaluation	test & slaughter	vaccination	hygiene methods & management practices	education campaign
- Resolution of Ministers Cabinet Nr. 7 (<i>Ministers cabinet of Mongolia, 1966</i>)	09.01.1966	Establishing the State Dispensary of Brucellosis	- establish a State Dispensary against Brucellosis within MoH					- allocate budget and provide staff;					
- Resolution of the Minister's Cabinet Nr. 448 (<i>Ministers cabinet of Mongolia, 1966b</i>)	21.12.1966	The results of prevention activities for animal glanders, brucellosis and tuberculosis;	- follow the Resolution Nr. 189/216, 172					- follow the Resolutions Nr. 189/216 & 172; - print the required documents to implement the tests;				- isolate infected animals; - compensate the herders for taking their private infected animals with healthy ones;	- organise a course for 100 lab workers; - create films & newspapers about the fight of glanders, brucellosis and tuberculosis;

Paper			Basic steps of Surveillance							Methods for control, eradication and prevention			
Term	year	Title	(i) objective	(ii) case definition	(iii) data collection	(iv) data analysis	(v) dissemination	(vi) implementation	(vii) evaluation	test & slaughter	vaccination	hygiene methods & management practices	education campaign
- Resolution of the Minister's cabinet Nr. 28 (Ministers cabinet of Mongolia, 1969)	31.01.1969	Measures to fight glanders, brucellosis & tuberculosis; collaboration with COMECON	- continue the activities to prevent glanders, brucellosis and glanders; - implementing the goal of reducing the prev. of brucellosis between 1969 and 1973;		- perform tests;		- report the results of the tests to the Ministers Cabinet;	- monitor the implementation of recommendations and plans; - support of local veterinary organisations; - provide supportive technical staff; - provide funds for material & staff from the central level; - strengthen the research laboratory for B in order to intensively develop scientific research and solve practical problems; - organise permanent transportation group;	- presentation on "the results of activities to prevent glanders, brucellosis & tuberculosis with the support of COMICON countries between 1966 and 1968": 37.5 mil animal tested and isolated inf. Animals, which led to a decrease of prev. In B of 50%; '- this under the help of COMICON Countries, local gov. cannot work sufficiently to eliminate animal infection; '- prev. B increased in Gobi-Altai, Bayan-Olgii, Khuvsgul & Selenge because they poorly segregated infect. animals.;			- monitor the isolation; - stop the breeding of male animals infected with B.; - organise state trade of horses, with tests; - train workers of agricultural unions, farms and veterinary field on lab test; - organise short course for 100 assistant veterinarians about preventing skills; - organise recommendations for prevention for the public;	

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Term	year	Title	(i) objective	(ii) case definition	(iii) data collection	(iv) data analysis	(v) dissemination	(vi) implementation	(vii) evaluation	test & slaughter	vaccination	hygiene methods & management practices	education campaign
- Director's order Nr. 17 of the National Institute for Hygiene, Epidemiology and Microbiology (National Institute for Hygiene, Epidemiology and Microbiology, 1970)	09.11.1970	- Guidelines of the vaccines to prevent human B.;						- support of the party	- study of epidemiological results of vaccination;		- vacc. of humans working in at-risk-places: workers in veterinary, with animal raw material, industries producing animal products, slaughterhouse s; staff; students working in lambing; herders; - transport and storage conditions for vaccines; - correct timing and dosage of vaccination; - test before vaccination;		- organise information about harm of B and effect of vaccination against B; - implementing guidelines on preventing of human B.";

Paper			Basic steps of Surveillance							Methods for control, eradication and prevention			
Term	year	Title	(i) objective	(ii) case definition	(iii) data collection	(iv) data analysis	(v) dissemination	(vi) implementation	(vii) evaluation	test & slaughter	vaccination	hygiene methods & management practices	education campaign
- Guideline of National Institute for Hygiene, Epidemiology and Microbiology Nr. 7/64 (<i>National Institute for Hygiene, Epidemiology and Microbiology, 1970a</i>)	Dec. 1970	- Guidelines for collaboration between human health and veterinary organisations to fight B;	- put B control under coordinated attention of human health and veterinary organisations;		- local MoH & MoA are jointly responsible for documenting the source of infection; - local MoH & MoA work jointly on investigation and lab tests;		- intersectional activities including conferences, workshops and meetings; - local MoH & MoA report to each other the occurrence of new cases and organise joint measures for the new infection source;	- permanent cooperation between MoH & MoA, also locally; - organise local committees for the coordination of planning, implementing and monitoring of the intersectional activities; - local MoH & MoA implement joint measures to eliminate the source of infection and preventative measures;					- coordinated health education for herders;

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Term	year	Title	(i) objective	(ii) case definition	(iii) data collection	(iv) data analysis	(v) dissemination	(vi) implementation	(vii) evaluation	test & slaughter	vaccination	hygiene methods & management practices	education campaign
- Joint order of MoH & MoA, Ministry of Education, Nr. 451/434/307 (Ministry of Agriculture et al, 1971)	01.11.1971	- Measures to intensify the prevention of B in Children and Youth	- implementation of the decision on the permanent measures on the prevention from B for the young people working in agriculture sector;		- submit a list of flocks containing infected animals to local gov.; - test people at risk twice;		- submit and discuss the results of the implementation of this order;	- local MoH & MoA jointly implement and supervise measures to fight B in coordinated actions;	- local MoH & MoA jointly evaluate the spread of B in humans and animals;			- supply protective cloths to herders, young people at risk etc.; - inform about suspicion of infection; - prohibit young people working in high risk farms;	- train school children working in agricultural sector on infection risks; - Local Mo Education organise distance education for school children on brucellosis, also print material;
- Order of MoA Nr. 267 (Ministry of Agriculture, 1972)	26.05.1972	-establish the testing detachment	- measures in order to eliminate animal brucellosis and glanders in near future;		- send testing groups; - count infected animals, also from previous year; -re-test newborns;		- discuss results of report and submit to the state committee;	- provide and assure transport facilities, technical experts, managerial support; - seminar for specialists to train methodology and management; - assign responsibilities for implementation and reporting; - assure funding for test, vaccination, logistics & management;	- scientists and specialists are sent to Aimags for advising, surveillance and commenting on progress; - supervision by veterinary specialists;		- provide 200'000 doses of S-19 for animals; -vaccinate people at high risk;	- segregate healthy animals;	

Paper			Basic steps of Surveillance							Methods for control, eradication and prevention			
Term	year	Title	(i) objective	(ii) case definition	(iii) data collection	(iv) data analysis	(v) dissemination	(vi) implementation	(vii) evaluation	test & slaughter	vaccination	hygiene methods & management practices	education campaign
- Joint Order MoH & MoA Nr. 205/290 (<i>Ministry of Agriculture et al.</i> 1972)	05.06.1972	- some measures to implement programme "Mongol - 0013";	- implement programme "Mongol 0013" (preliminary preparation to produce Rev-1);					- implement programme "Mongol - 0013", organise the management responsibilities, coordination with WHO, logistics, human resources, assure funds;					
- Resolution of Ministers Cabinet Nr. 362 (<i>Ministers cabinet of Mongolia.</i> 1972)	08.09.1972	- Rules for treatment of people with Brucellosis;						- reorganisation of B responsibilities within MoH; - responsibilities of MoH & MoA for reporting on the implementation programme to fight B;			- revising the rule of free treatment against B in outpatient facilities;		
- Resolution of the Minister's Cabinet Nr. 95 (<i>Ministers cabinet of Mongolia.</i> 1974)	15.03.1974	- Production of vaccine to prevent B	- to implement the "Mongol-0013" programme to produce the vaccine against B.;					- assuring funds; - establishing head committee for the programme;			- MoA is responsible to establish production of Ref-1 vaccine;		
- Order of MoA, Nr. 286 (<i>Ministry of Agriculture.</i> 1975)	19.07.1975	- about vaccinating animals with Rev-1;	- to introduce Rev-1 vacc. produced in Mongolia;		- keep detailed registration of animals vaccinated;		- report result of the survey to the Minister's council;	- approve amount of vaccine, manpower, transport facilities, equipment; - approve schedule; - assure financing of the Rev-1;	- conducting epizootiological survey on immunisation; - conduct a post vaccination survey;		- vacc. Sheep & goats of Bulgan & Selenge from 20.7. to 15.8.;	- preventative measures among the local population;	- Seminar for staff on how to use, store, transport vaccine Rev-1 and on reporting system;

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Term	year	Title	(i) objective	(ii) case definition	(iii) data collection	(iv) data analysis	(v) dissemination	(vi) implementation	(vii) evaluation	test & slaughter	vaccination	hygiene methods & management practices	education campaign
Order of MoA Nr. 277 (Ministry of Agriculture, 1976)	17.07.1976	about vacc. of sir by Rev-1	- in order to organise effective and efficient prevention from B by using Rev-1;	- monitor the process of diagnosis of B;	- keep detailed registration of animals vaccinated; - diagnose blood and placenta of sheep & goats with abortion to define epizootic.		- report result of the survey to the Minister's council; - conduct dissemination and promotion activities on importance of the vaccination campaign and labour safety & staff; - final reports on the vacc;	- approve amount of vaccine, manpower, transport facilities, equipment; - approve schedule; - assure financing of the Rev-1;	- to develop & adopt guidance on how to conduct epidemiological monitoring & hygiene after vacc.; - to evaluate process of epizootic after vacc with 20% of all vacc. animals; - monitor the process of diagnosis of B; - diagnose vacc. Animals after 2 years;	- slaughter aborting animals caused by brucellosis and animals with suspicious test results; Bayan-Olgii, Dornod & Sukhbaatar & all new born sheep & goats in Bulgan & Selenge Aimags from 25.7. to 15.8.; - dose: 2 millions per sir;	- vacc. all female sheep & goats of all age 1-2 months prior to mating in the Aimags Bayan-Olgii, Dornod & Sukhbaatar & all new born sheep & goats in Bulgan & Selenge Aimags from 25.7. to 15.8.; - dose: 2 millions per sir;	- Pre vaccination measures: reduce diagnostic procedure and put more attention to hygiene procedures such as: registration of the animals, conduct proper surveillance and keep same epizootic, keep new born separately, separate animals with abortion, disinfect corrals and fences, burn or dig placenta, keep animals giving birth separately; - guidance for storage of Rev-1; - mark vacc animals;	- Seminar for staff on how to use, store, transport vaccine Rev-1 and on reporting system;

Paper			Basic steps of Surveillance							Methods for control, eradication and prevention			
Term	year	Title	(i) objective	(ii) case definition	(iii) data collection	(iv) data analysis	(v) dissemination	(vi) implementation	(vii) evaluation	test & slaughter	vaccination	hygiene methods & management practices	education campaign
- Resolution of Ministers Cabinet Nr. 320 (<i>Ministers cabinet of Mongolia, 1977</i>)	18.11.1977						- Local Gov. is responsible to discuss results & implement planning; - MoH is responsible to establish the State Dispensary of Brucellosis (incl. monitoring, investigating laboratory quality for Rev-1); - MoH is responsible to establish mobile groups to investigate spread of B, diagnose & treat people, organise & monitor preventive measures; - MoH is responsible to provide staff; - local gov. is responsible to implement rules such as prevention, vacc. of people at risk and investigating B ;						

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Term	year	Title	(i) objective	(ii) case definition	(iii) data collection	(iv) data analysis	(v) dissemination	(vi) implementation	(vii) evaluation	test & slaughter	vaccination	hygiene methods & management practices	education campaign
- Order of MoH Nr. 346 (Ministry of Health, 1977)	26.12.1977	- Some measures to fight B;	- implement resolution Nr. 320 ;				- send specialists to study the experience on fighting and preventing B in the Kazakh Area of the Soviet Union and invite these specialists to the planning; - report with the results of activities and implementation process;	- MoH is responsible to establish the State Dispensary of Brucellosis (incl. monitoring, investigating laboratory quality for Rev-1; - MoH is responsible for administrative work and centralised management to prevent and fight B.; - establish local permanent mobile groups to fight B in Aimags; - allocate budget, assure funds, provide transport facilities, office space, equipment and drugs; - Coordination between MoH, local Government and directorates;	- Monitoring of the guidelines for fighting, preventing, diagnosing and treatment of B; -				- organise a seminar for physicians of the permanent mobile groups on prevention of human B; - broadly publishing and distributing of posters, materials, lectures, recommendations to prevent & fight B;
- Order of MoH Nr. 207, out of (Enkhbaatar L et al, 2004), did not find	26.07.1978	- for medical workers who are responsible for monitoring patients with chronic											

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Term	year	Title	(i) objective	(ii) case definition	(iii) data collection	(iv) data analysis	(v) dissemination	(vi) implementation	(vii) evaluation	test & slaughter	vaccination	hygiene methods & management practices	education campaign
- Resolution of the Minister's Cabinet Nr. 29; out of (<i>Enkhbaatar L et al, 2004</i>), did not find original;	26.01.1979	- on separating the cattle with brucellosis on mechanised milk farms											
- Order of MoH Nr. 70 (<i>Ministry of Health, 1979</i>)	07.03.1979	- some measures to intensify the activities to fight and prevent B;	- new orders because the implementation of the order Nr. 346 & Nr. 320 were poor;		- list names of people working in lambing;		- assuring reporting to MoH; - organise lectures and discussions, distribute the recommendations and produce posters;	- centralising the activities against B; - develop direct cooperation with Research Institute of Microbiology and Infection Disease of Kazakh State; - develop collaborative work with veterinary and other community organisations on prevention;	- supervise and advise on the implementation of guidelines; - supervise and advice occupational conditions of herders and seasonal workers working in at risk farms;		- test and vaccinate healthy people before working in lambing;	- provide diagnostic preparation for humans; - submit names of people working in lambing to the local health authorities and organise prevention vaccination; - provide protecting equipment to people working in lambing; - prepare disinfection substances for the period of lambing; - physical examination of people after working in lambing; - prohibit unvaccinated and untrained people form participating in the work of lambing; - monitor disinfection of site and disposal of aborted foetuses;	- organise training for people working in lambing;

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- Resolution of the Minister's Cabinet Nr. 307, out of <i>(Enkhbaatar L et al, 2004)</i> , did not find original;	1979	- some measures for receiving, transferring and purchasing milk											
- Order of the MoA Nr. 138/40 <i>(Ministry of Agriculture, 1982)</i>	13.04.1982	- Establish the committee to perform the tests, and conduct the elimination of B in cattle of dairy farms;	- implement the resolutions Nr. 140 & 91 <i>(comment: we could not find these two resolutions)</i> ;		- monitoring testing of cattle in dairy farms and of bulls used for breeding;		- certificate healthy dairy farms; - submit the reports for distributing the certifications after monitoring tests;		- supervise the measures for veterinary - sanitation conditions and quarantine; - discuss the results of monitoring tests with Veterinary Directorate Office;			- protect not infected cattle dairy farms; - supervise testing materials and use (slaughter, eliminating, segregating) of infected cattle;	

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- Addition 1 for Agreement Nr. 7202151100 (Ministry of Agriculture, 1986)	15.10.1986	- Additional issues on an agreement between the Government of the Soviet Union and the Government of Mongolia on economical and scientific technology collaboration between 1986 and 1990;	- Russia supplies technical veterinary support and equipment to Mongolia in order to fight B in milk farms in Mongolia;					- supply of equipment;					

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Term	year	Title	(i) objective	(ii) case definition	(iii) data collection	(iv) data analysis	(v) dissemination	(vi) implementation	(vii) evaluation	test & slaughter	vaccination	hygiene methods & management practices	education campaign
- Order of the MoA Nr. A/144/44 (Ministry of Agriculture, 1987)	10.04.1987	- Implementation of Resolution Nr. 246 (some measures to prevent cattle B) (<i>we did not find this resolution</i>);	- prevent B in cattle; - diagnosing the animal infection in diary farms and organise measures against B in cattle;	- expedition director is responsible for organising the group work and advising for the testing of RB, CFT & SAT and for methodology;	- study prevalence of B in cattle milk farms in 7 Aimags through expedition team in cooperation with Russia; - perform bacteriological tests in aborted foetuses;		- Seminar among veterinarians and specialists working in this survey; - report the results to Ministry; - distribute the experience of veterinary offices, administrative and management work in fighting animal B;	- implement activities on prevention and elimination of cattle b; - supply administration management for joint expedition team between Mongolia and Russia; - supply equipment for labs, transport facilities; - assure funds; - establish places for testing; - staff members on of the Committee against animal and human brucellosis; - establish the joint expedition team of Mongolia and Russia against cattle B in some Aimags with diary farms; - assure access of the specialists to the diary farms;	- supervising and controlling permanently the process of tests, vaccination; - collect implementation report; - organise state veterinary supervision;	- isolated infected animals and send them to slaughter;	- S-19 vacc. Of uninfected cattle after final tests of B; - establish special flocks with vaccinated cattle;	- provide protecting clothes for people working in the survey;	

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Term	year	Title	(i) objective	(ii) case definition	(iii) data collection	(iv) data analysis	(v) dissemination	(vi) implementation	(vii) evaluation	test & slaughter	vaccination	hygiene methods & management practices	education campaign
- report on the expedition to prevent B in 1987 <i>(Ministry of Agriculture, 1988)</i>	1987	- Report on the work of the Mongolian-Russian Expedition to prevent B in 1987 in 7 Aimags;	- in order to implement Resolution 176/196 of July 1970;	- first serological tests of SAT, CFT & RB , second test through blood sampling;	- 682'800 cattle tested twice, included Aimags: Tuv, Selenge, Arkhangai, Dornod, Bulgan, Khuvsgul, Khentee); - 59'000 sheep, 6'000 goats & 6'200 camels tested;			- Soviet Union sent specialists, cars & trucks, equipment, testing materials, vaccines (S-19);		- 91% of seropositive animals were isolated and slaughtered;	- vaccinate cattle in diary farms with S-19 in Tuv & Selenge, with Rev-1 in Arkhangai, Dornod, Bulgan, Khuvsgul, Khentee;		

Paper			Basic steps of Surveillance							Methods for control, eradication and prevention			
Term	year	Title	(i) objective	(ii) case definition	(iii) data collection	(iv) data analysis	(v) dissemination	(vi) implementation	(vii) evaluation	test & slaughter	vaccination	hygiene methods & management practices	education campaign
- report on the expedition to prevent B in 1988 <i>(Ministry of Agriculture, 1988)</i>	1988	- Report on the work of the Mongolian-Russian Expedition to prevent B in 1988 in 7 Aimags;		- primary tests with SAT, CFT & RB, repeated tests	- 240'057 cattle tested twice in four Aimags (Zavkhan, Uvurkhangai, Bayankhongor, Sukhbaatar)				- study on post-vaccination reaction in the vaccinated cows in 1987 in the 7 Aimags, with result: after 10 months re-titres in 1/400 by SAT & 1/40 by CFT;	- 84% of seropositive animals were isolated and slaughtered;	- vaccination of 240'000 cows with Rev-1 in Zavkhan, Uvurkhangai, Bayankhongor, Sukhbaatar; - vacc. In 11 Aimags (7+4) 27'792 camels, 142'000 sheep, 27'279 goats, dogs & pigs;		

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- MoA, methodology paper (<i>Badarch P., 1988</i>)	01.06.1988	- testing methodology of the joint team between Mongolia & Soviet Union to prevent B in 1988;	- methodological details on the implementation of the joint Mongolian - Russian programme;	- female cows will be tested by SAT (1:100,), CFT (1:5) and seropositive blood sampling of them will be performed by SAT (1:50, 1:100, 1:200, 1:400) and by CFT (1:5, 1:10, 1:20). In analysing the test results, the methodological committee will discuss and decided future vaccination and testing of these animals;	- investigating the infection level in 11 Aimags with 3 test combination in cattle, camels, male animal used for breeding, dogs & pigs;	- study infected animals by age group and sex and discern the segregated herds;	- regularly explain to local leaders & specialists the necessary requirements of diagnostic tests and their economic benefits; - develop the protocol and discuss the results in local government.;	- introduce methodology to the specialists of the expedition team before beginning with testing;	- register diagnostic tests, analyse monthly reports, report to authorities in charge;	- see report above;	- see report above; - supervise vaccine storage and duration of the vaccines;	- prohibit use of single needle for many animals;	

Paper			Basic steps of Surveillance							Methods for control, eradication and prevention			
Term	year	Title	(i) objective	(ii) case definition	(iii) data collection	(iv) data analysis	(v) dissemination	(vi) implementation	(vii) evaluation	test & slaughter	vaccination	hygiene methods & management practices	education campaign
- Presentation (<i>Badarch P., 1988a</i>)	1988	- Presentation of Dr. P. Badarch, about the Russian aid in fighting Brucellosis;				- study progress of human and animal B;	- submit report of programme implementation to the Government;	- hint on difficulties in the implementation, such as: insufficient organisation of the veterinary management, equipment and vehicles not maintained, methodological mistakes, low effectiveness of the vaccines, uncompleted isolation of seropositive animals;					
- Government Resolution (<i>Ministry of Agriculture et al, 1991</i>)	1991	- National programme to fight human and animal B 1992 - 1995	- fight against B in human and animal;					- survey & research related to introduction of new methods of diagnosis, treatment and prevention; - establish a National Council in charge of coordination of the different organisations concerned by the fight of B; - introduce new international diagnose methods in animals and humans; - assure funds, transport, equipment, logistics;		- slaughter infected animals, certificate herds, sums, bags without infected animals;	- vaccinate animals;	- coordination of events in human (treatment, prevention) and in animals (testing, slaughtering);	

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- Minutes of the Cabinet Meeting (Ministry of Agriculture et al, 1992)	07.02.1992	- National Programme to fight against human & animal B of 1992 - 1995; - Annexe to of the minute;	- reduce prevalence in human and animal brucellosis;	- define Brucellosis epizootiology;	- develop database on prevalence in human and animal B. at the level of National Council; - conduct a survey among 153'000 herders; - diagnose B among cows of farms; - diagnose reasons for abortion among all animals; - diagnose B in sir in certain Aimags according to the schedule;		- hand over certificates according to the level of infection of the herd; -	- implement programme, assure funds, establish organisation; - conduct surveillance of human and animal B; - conduct a survey on epidemiology of human B and develop guidance on measurement; - introduce appropriate methods on diagnosis and treatment; - conduct research on human & animal B and prevention methods; - train specialists on B; - establish National Council at MoH in charge of implementing programme, also involve local Gov; - develop international cooperation and exchange of specialists; - Improve collaboration between Health Department and Veterinarian Department; - improve and organise research on Brucella Bacteria;	- conduct research on improving the methods of diagnosis, treatment and prevention; - study epizootiology and epidemiology of B, to define biological and immunisation mechanism; - study effectiveness of the vaccine;	- test animals and slaughter infected animals; - fatten infected animals and slaughter them;	- vaccinate young cattle with S-19 in Tuv & Selenge, and with Rev-1 in other Aimags (except Umnogobi); - revaccinate the cows vaccinated in 1987 - 89; - if necessary vaccinate all sheep & goats of all ages with Rev-1;	- treat patients with infection and improve treatment; - provide protecting equipment to workers at risk; - mark products from infected animals; - use healthy animals for mating, test male animals before mating; - study risk of exposure, develop proper methods for prevention;	- permanent training of medical staff and veterinarians; - dissemination of activities for general population through movies, leaflets, handbooks; -

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- official letter from city gov. to MoA Nr. 4/467 <i>(Veterinary state general supervisor, 1992)</i>	23.03.1992	- safety of the milk for the population of UB;	- recommendation to implement the measures as decided by government in Feb. 92;									- do not provide infected milk;	
- Order of MoH & MoA Nr. A746/11 <i>(Ministry of Agriculture et al, 1992b)</i>	01.04.1992	- Attachment III concerning Guidelines to fight animal and human brucellosis;	-		- testing: diagnose human & animal B by bacteriological serological methods, allergic tests and observing syndromes; - apply RB, CFT, and SAT (Allergic test in sr & pigs); - description of interval of testing;			- local governm.. plan and organise activities against human & animal B; - plan of local gov. should include: testing, vaccination, separation of infected animals, slaughter, administration, management, animal movement restriction, education among herders and persons at risk; - community (sums, bas, farms) provide transport facilities, manpower, equipment; - local vet. authorities carry out the implementation, and do supervision;	- in order to identify immunisation of vaccinated animals test with SAT blood (10%) in proportion 1:100, 1:200 15 to 21 days after vaccination;	- t & s animals in high risk regions/farms (<1%); - re-test bulls at intervals of 30 days; - t & s dogs once a year; - t & s camels;	- vacc. healthy animals in on farms with infection level >1%;	- prohibit untested animals to join flocks (twice testing with SAT, CFT & RB plus certificate them); - isolate infected cattle and cattle flocks; - create new farms with tested and vaccinated female and allow to mate; - mark infected animals; - boil milk of infected cattle or pasteurise milk from infected farm; - wait 2-3 months before using feed, pasture and water of rivers of infected animals; - slaughter animals with abortions;	

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												<ul style="list-style-type: none"> - disinfect environment where cattle give birth, as well winter and spring campus; - improve the individual hygienic and sanitary conditions of herders, veterinarians and physicians should sustain and control; - workers in places with infected animals should use protecting clothes and equipment, disinfection and pharmacy; - only vaccinated people should work in fighting B; - slaughter of infected animals requires necessary hygiene, sanitation and disinfection; - compliance with law on implementation of veterinary, sanitary and administrative activities; 	

Paper			Basic steps of Surveillance							Methods for control, eradication and prevention			
Term	year	Title	(i) objective	(ii) case definition	(iii) data collection	(iv) data analysis	(v) dissemination	(vi) implementation	(vii) evaluation	test & slaughter	vaccination	hygiene methods & management practices	education campaign
- Joint order MoA & MoA Nr. A/46/11 (<i>Ministry of Agriculture et al, 1992c</i>)	08.04.1992	- to implement the programme about measures to fight the human & animal B in 1992 - 1996;						<ul style="list-style-type: none"> - implement sub-council to fight B; - working instruction to prevent, diagnose & treat human & animal B; - delegation of responsibilities to the sub council like planning, management, dissemination of results, international collaboration; - establish a methodological group to fight B; - assure transport, funds, technical information; - organise training; - investigate the risk group; - organise the work in a joint team of specialists, laboratory, machinery in human and animal sector; 					

Paper			Basic steps of Surveillance							Methods for control, eradication and prevention			
Term	year	Title	(i) objective	(ii) case definition	(iii) data collection	(iv) data analysis	(v) dissemination	(vi) implementation	(vii) evaluation	test & slaughter	vaccination	hygiene methods & management practices	education campaign
- Resolution of Gov. Nr. 119 (<i>Ministry of Food and Agriculture, 1996</i>)	18.05.1996	- programme to fight human & animal B between 1996-2000;	- systematically eliminate the infectious source in Tuv, Selenge and UB with local and international funding and develop new methodologies to fight B;		- investigate the spread of B in human & animals, and high risk groups in Tuv, Selenge & UB;		- local health & vet. organisations report to methodology committee, which discuss and report to MoH, MoA and State Gov.;	- local gov. & govern. of UB are responsible for financing the measures: - MoH & MoA are responsible for providing the programme, administration, professional and methodological management; - international cooperation and financing has to be searched; - implement programme in Tuv, Selenge & UB with some financial support, other Aimags have to fund themselves; - establish professional & methodological committee with scientists and specialists for human & animal health for monitoring and organising the activity; - support scientific research on human & animal B and recommendation on prevention B;		- minimum annual testing: 100'000 persons & 2.3 mil. Animals; - slaughter infected animals;	- vaccinate uninfected animals with S-19 and Rev-1; - vaccinate as experiment pigs with Suis-2 in Tuv;	- implementing measures in prevention: - treat patients with modern methods; - develop sanitation control on meat, milk and animal raw products; - isolate infected animals; - compensate for slaughter of infected animals; - certificate healthy agricultural organisations;	- train lab. specialists; - workshops with local leaders, medical doctors, veterinarians on future aims, management and methodology;

Paper			Basic steps of Surveillance							Methods for control, eradication and prevention			
Term	year	Title	(i) objective	(ii) case definition	(iii) data collection	(iv) data analysis	(v) dissemination	(vi) implementation	(vii) evaluation	test & slaughter	vaccination	hygiene methods & management practices	education campaign
- Joint order between MoH & MoA Nr. A/199 A/78 (<i>Ministry of Agriculture et al, 1997</i>)	26.05.1997	-	- intensify the implementation of resolution Nr. 119;				- each Aimag should send report in November to Sanitary and Veterinary State Laboratory;	- establish the committee and charge to implement the measures: cooperation plan, international assistance, experiment with vacc. Suis-2, report to MoH 6 MoA; - charge RCHID: supply drugs, medication, lab materials & profess. Administration, inform on data collection, supply budget for lab testing of risk groups; - charge local health organisations: establish permanent groups to fight B, follow the programme;					

Paper			Basic steps of Surveillance							Methods for control, eradication and prevention			
Term	year	Title	(i) objective	(ii) case definition	(iii) data collection	(iv) data analysis	(v) dissemination	(vi) implementation	(vii) evaluation	test & slaughter	vaccination	hygiene methods & management practices	education campaign
- Resolution of government Nr. 64 (Ministry of Agriculture, 1999)	21.04.1999	- to assign the local governments to implement the programme and report to the committee;	- to protect animals and improve quality of the service by prevention from the zoonotic diseases of category A in order to avoid socio-economic losses and to increase export rate;		- conduct surveillance of animal B.....at household level;			- the programme will be implemented in 1999 - 2010 in 3 phases: First phase 1999 - 2000 development of legislation, structure of veterinary services (privatising, capacity building), improve epidemiological activities. Second phase 2000 - 2005: conduct nationwide surveillance to define B, TB, glanders leucosis and infectious anaemia of horses, to undertake measures to be included in the list of countries free from foot & mouth, plague and measles in horses, establish quarantine at border, improve bio factory and laboratory, seek funding. Third phase 2005 - 2010: Eliminate B, TB, leucosis, anaemia of horses, development of strategies to monitor, fight & prevent these diseases;				- improve prohibition and monitoring at the border pass; - improve readiness of veterinary services at all levels in case of emergency; - improve stockpiling of medical equipment; - protect animals; - ensure food safety; - improve hygiene; - improve diagnostic; - prepare veterinary department for international licensing; - formulate legislative & economic condition for private sector to run veterinary services; - improve capacity building of veterinary services; - improve monitoring service of veterinary departments at all level; - implement prevention for animals;	

Paper			Basic steps of Surveillance							Methods for control, eradication and prevention			
Term	year	Title	(i) objective	(ii) case definition	(iii) data collection	(iv) data analysis	(v) dissemination	(vi) implementation	(vii) evaluation	test & slaughter	vaccination	hygiene methods & management practices	education campaign
- Order of MoA Nr. A/101 (Ministry of Agriculture, 2000)	10.07.2000	- Order to implement Gov. Resolution Nr. 64;			- MoA & local gov. shall perform the surveillance & monitoring to investigate B in camels, cattle, sheep & goats;			- local Gov. is responsible for financing vaccination and tests;	- surveillance and monitoring tests; - - Local Gov. establish and send working groups with animal and human health specialists for advising, monitoring and evaluating testing and vaccination;		- vaccinate animals		
- Guidance to vaccinate animals against B (Ministry of Agriculture, 2000a)	10.08.2000		- to implement Resolution of Gov. and order of MoA Nr. A/101 in order to reduce prev of B;				- reports on the vaccination;		-		- vaccinate animals from 15.8. to 15.9.; - vaccinate 5.3 mil. animals of 11 Aimags; - store vaccines according to the requirements;	- supply dairy products and animal raw products to the market from the households that fully involve their animals to the vaccination campaign; - strictly monitor all the movements of animal; - check all animals coming from other Aimags;	

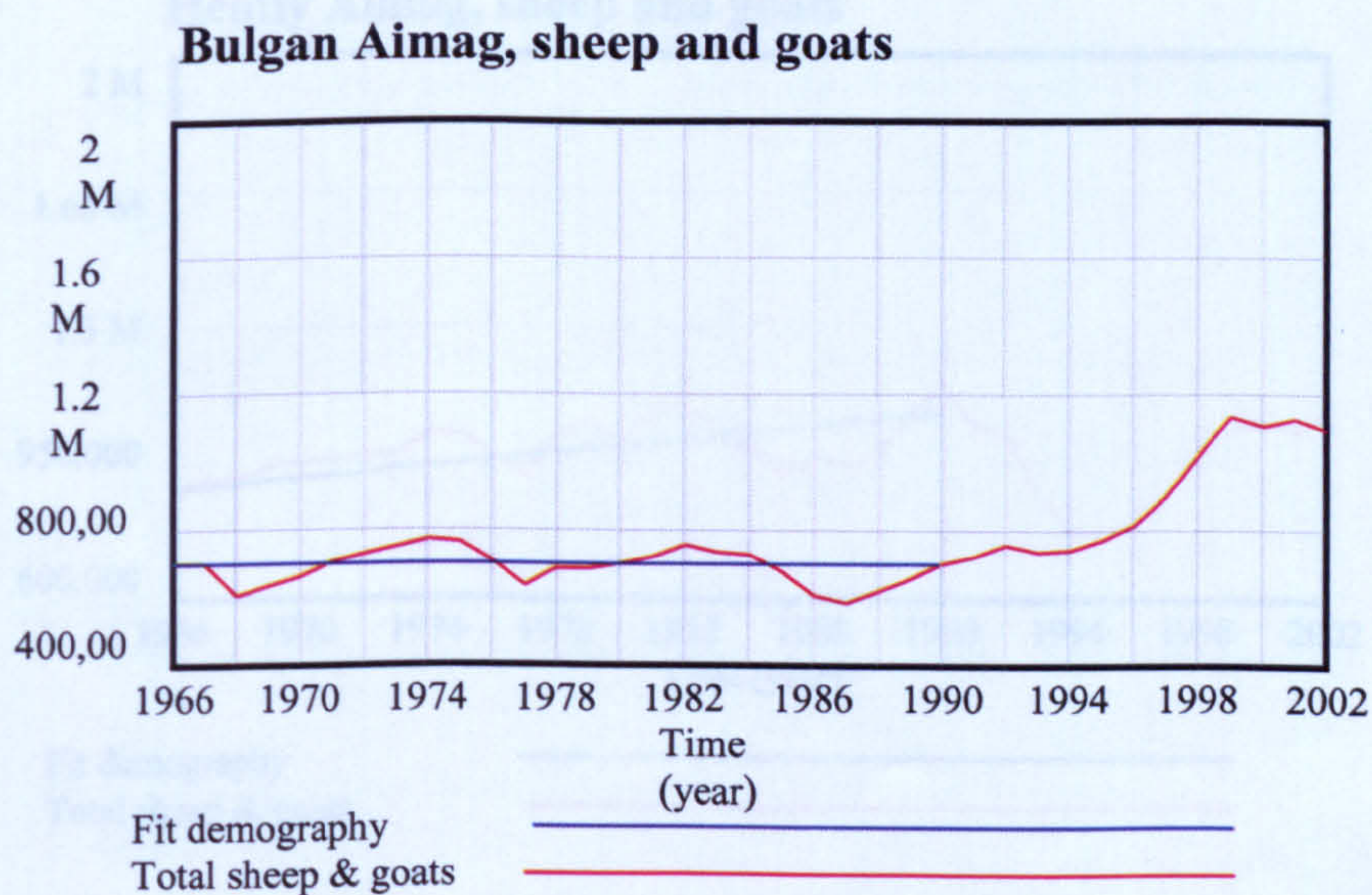
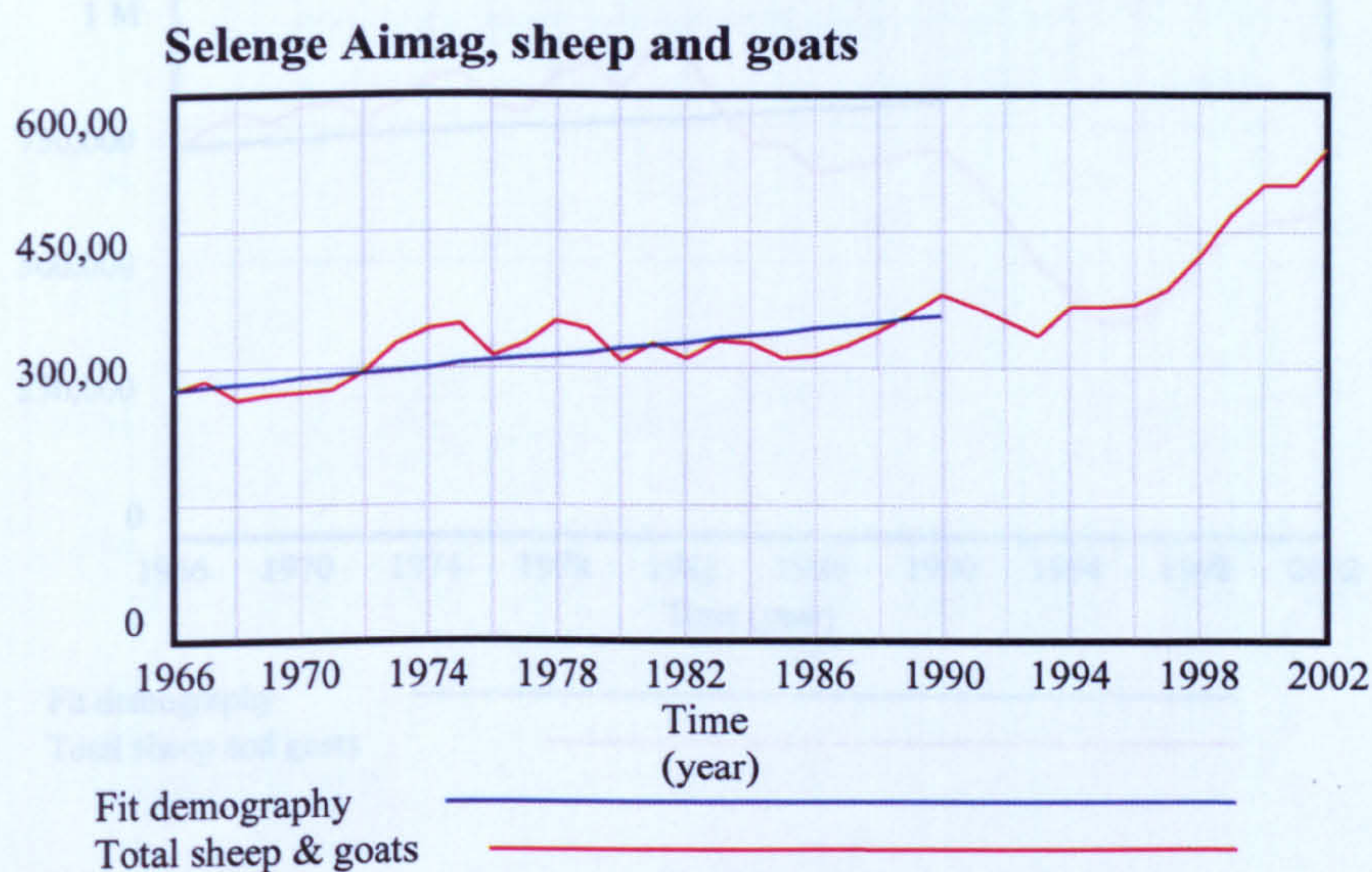
Paper			Basic steps of Surveillance							Methods for control, eradication and prevention			
Term	year	Title	(i) objective	(ii) case definition	(iii) data collection	(iv) data analysis	(v) dissemination	(vi) implementation	(vii) evaluation	test & slaughter	vaccination	hygiene methods & management practices	education campaign
- Order of MoA Nr. A/08 (Ministry of Agriculture, 2000b)	31.08.2000	- about experimenting with vaccine B.abortus 159 No.5R;			- study prev if bovine B in concerned region in order to compare experiment with pre-vaccination;						- experiment with vaccine B.abortus 159 No. 5R;		
- Resolution of Mongolian Gov. Nr. 206 (Ministry of Agriculture, 2001)	19.09.2001	- Ordering the measures considering implementing the projects "Fighting B in cattle, sheep & goats";					- MoA is responsible for collecting the results from each Aimag and report to the government;	- MoA is responsible to implement the project; - the MoA & MoF are responsible to implement the measures & to assure the required funds with support of international sources;					

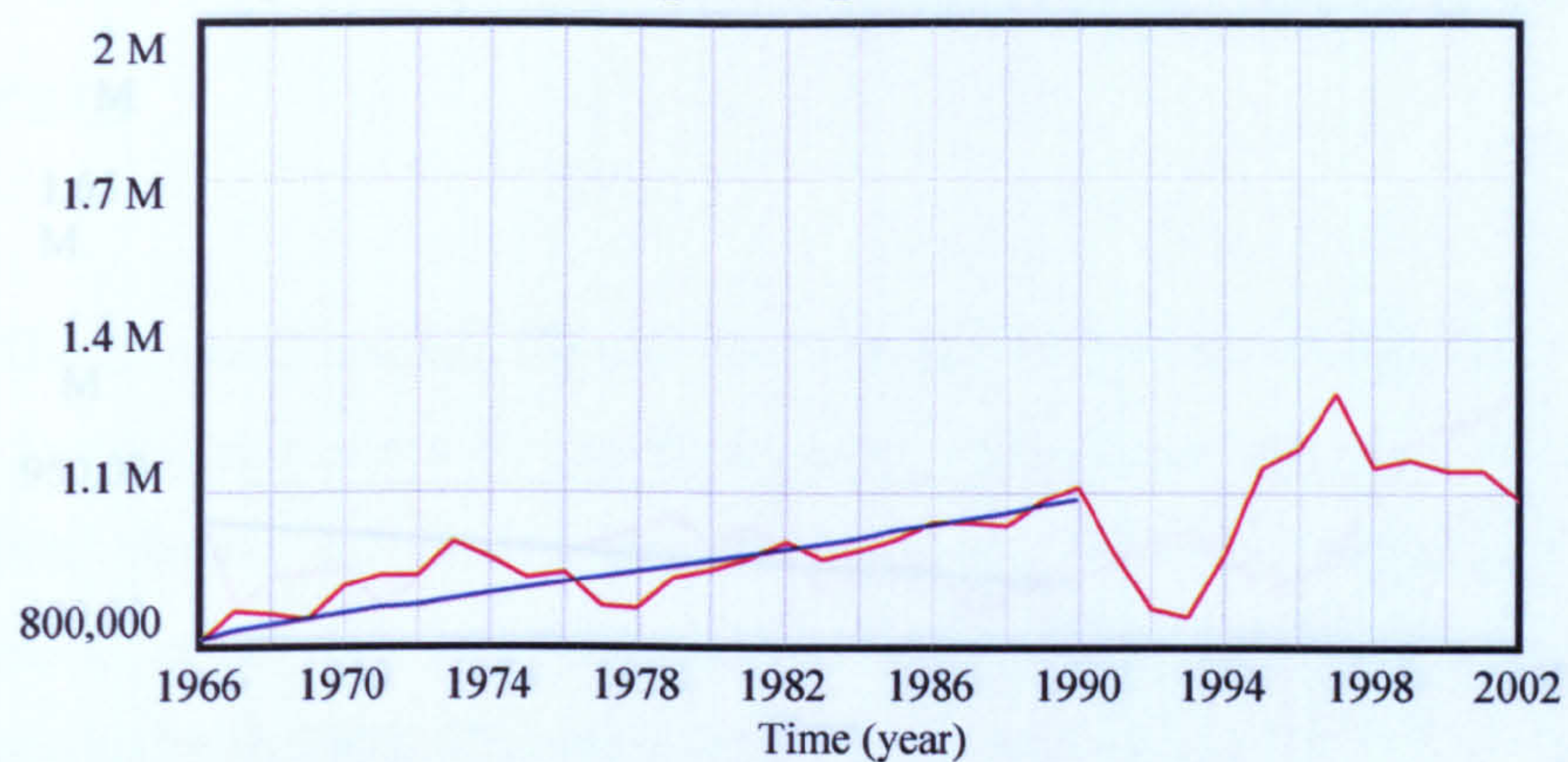
Paper			Basic steps of Surveillance							Methods for control, eradication and prevention			
Term	year	Title	(i) objective	(ii) case definition	(iii) data collection	(iv) data analysis	(v) dissemination	(vi) implementation	(vii) evaluation	test & slaughter	vaccination	hygiene methods & management practices	education campaign
- Project plan of State Veterinary & animal breeding department, MoA (State Veterinary & Animal Breeding Department of the Ministry for Food & Agriculture et al, 2001)	- 2001	- Combating against brucellosis in cattle, sheep and goats	- to enhance the curing and prevention of livestock form brucellosis.		- monitoring in starting year, with 10% of sr and 20% of cattle, all over Mongolia;		-	<ul style="list-style-type: none"> - During 10 years vaccination every year of the new born female kids and lambs with Rev-1 and calves with S19; - Within 3 years vaccination of all breeding adult females cattle (with S19), sheep and goats (with Rev-1), and repeat of this vaccination 3 years later; - Assess of the vaccination success through a survey before the repeated vaccination; - Mark of all vaccinated animals (ear tag); - Testing breeding males twice a year and slaughtering of the reactors; - Surveillance through detecting the infection level in herders and other risk groups. 			whole herd vacc campaign for 10 years		- training and seminar with veterinarians and medical doctors.

Paper			Basic steps of Surveillance							Methods for control, eradication and prevention			
Term	year	Title	(i) objective	(ii) case definition	(iii) data collection	(iv) data analysis	(v) dissemination	(vi) implementation	(vii) evaluation	test & slaughter	vaccination	hygiene methods & management practices	education campaign
- Resolution of Mongolian Gov. (<i>Prime Minister of Mongolia et al, 2002</i>)	28.06.2002	- approval of "National Programme Control of Communicable Diseases"	- count as invalid Res. 119 from 1996; - the control of infectious diseases still remains as one of the essential issue of public					- MoA: in cooperation with other institutions organise and take preventive and control measures against animal originated infectious disease like brucellosis, anthrax, echinococcosis and tuberculosis.					
- Programme activities (<i>Ministry of Health, 2002</i>)	- 2002	- Sub programme for prevention and control against zoonosis and natural foci diseases	- programme organisation concerning the sub programme for prevention and control of brucellosis;				- improvement of surveillance and information network on brucellosis	- improvement of participation and collaboration of sum and family doctors, governmental and non governmental organisations in fighting against brucellosis;					- improvement of education & training among the population on brucellosis;
- Resolution of Gov. Nr. 223 (<i>Ministry of Agriculture, 2002</i>)	06.11.2002	- about implementing the projects to fight some animal infectious diseases;					- MoA is responsible for collecting the results from each Aimag and report to the government;	- MoA, MoF & the local governments are responsible for allocating the required funds in local budgets and including assistance from donor countries; - MoA is responsible to implement the project;					

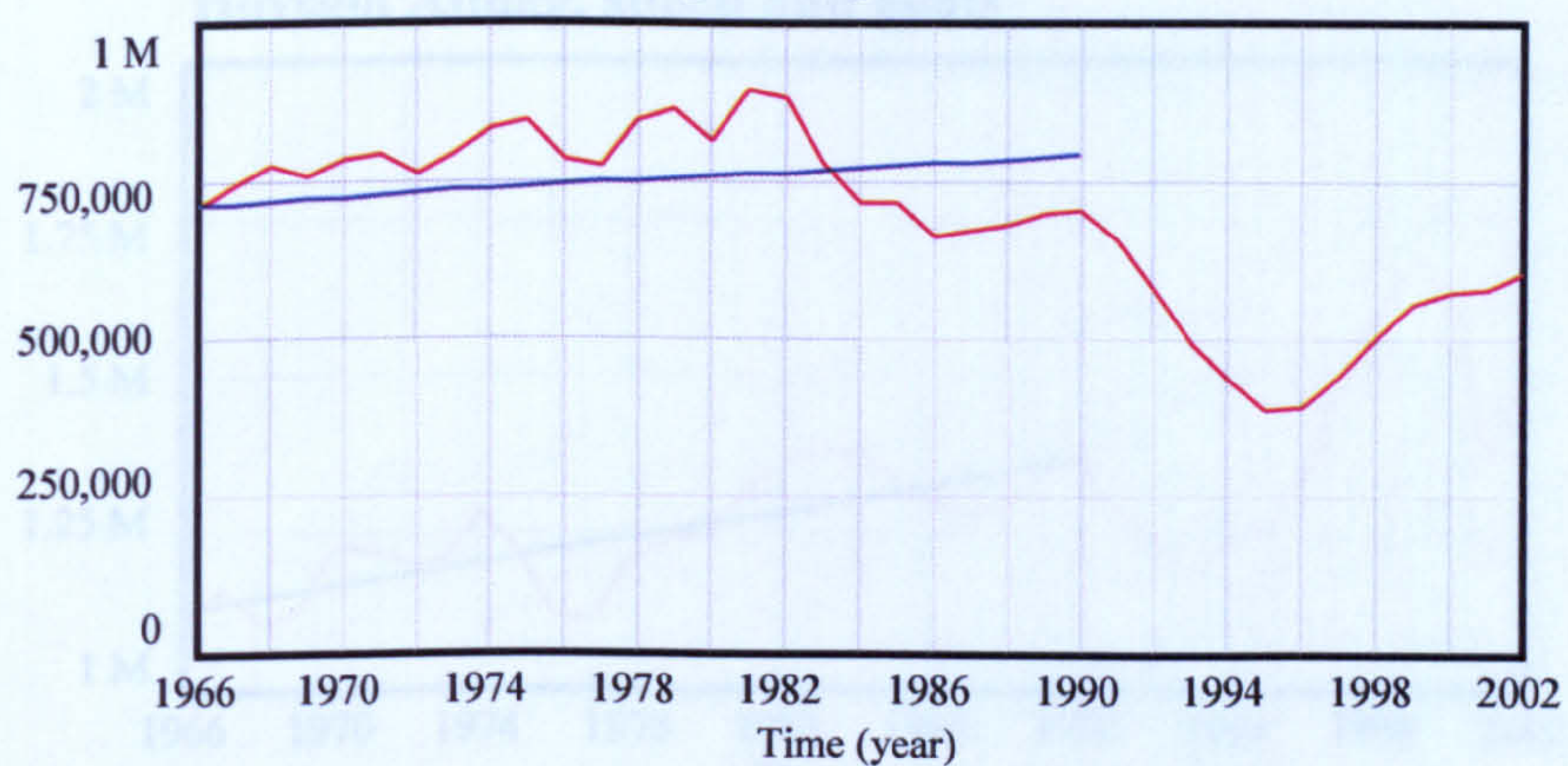
Appendix 6.2.: Mathematical fit of the demographic parameters

The demographic fit to the real data of the populations in small ruminants was done for the time period 1966 to 1990. The initial birth rate (α) was set at $0 \leq \alpha = 0.8 \leq 2$, and the initial mortality rate (μ) at $0 \leq \mu = 0.8 \leq 1$. With this the most likely range was defined according to previous work (Zinsstag *J et al*, 2005). The data are derived from material collected for this thesis.

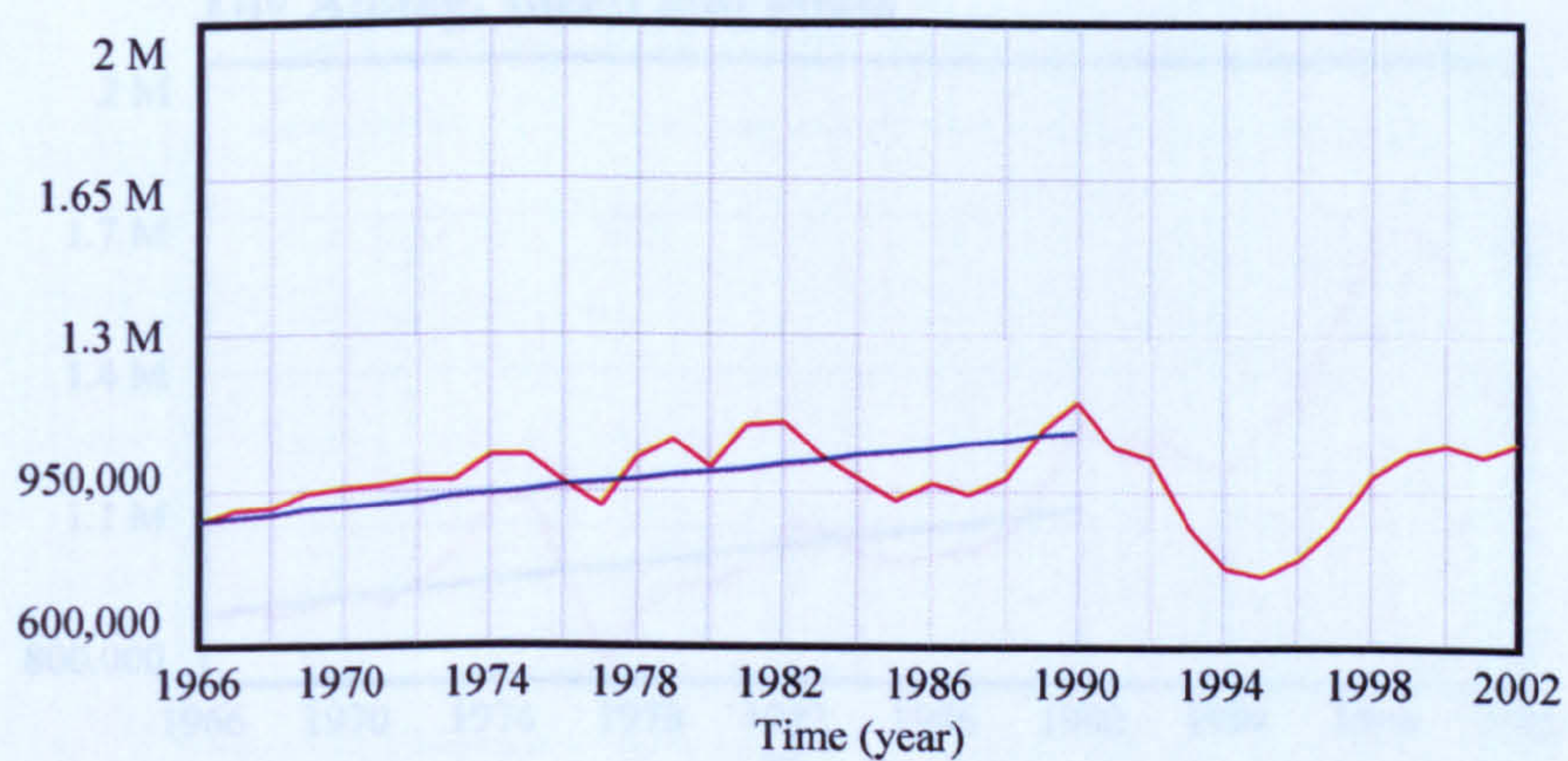


Bayan-Olgii, sheep and goats

Fit demography
Total sheep & goats

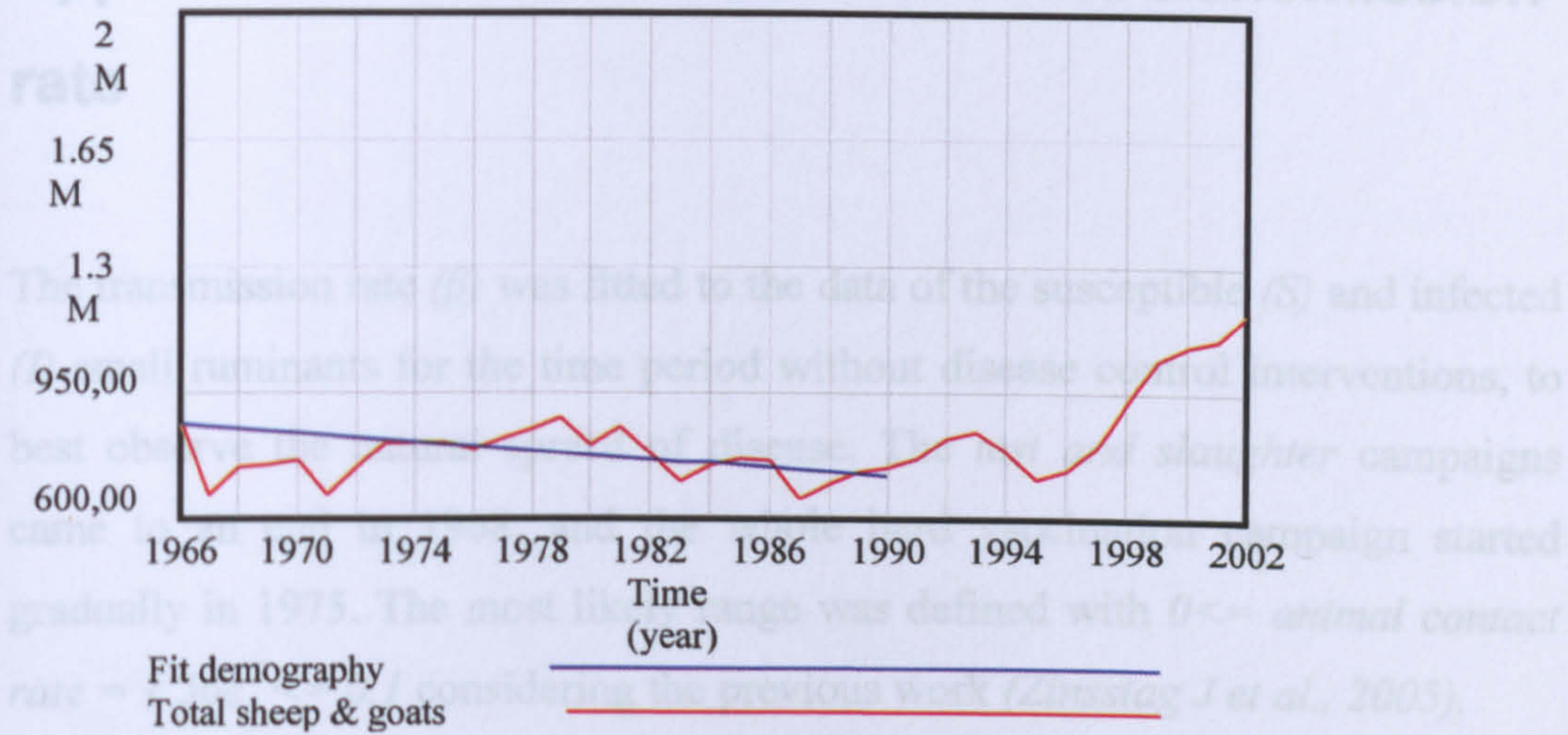
Dornod Aimag sheep and goats

Fit demography
Total sheep and goats

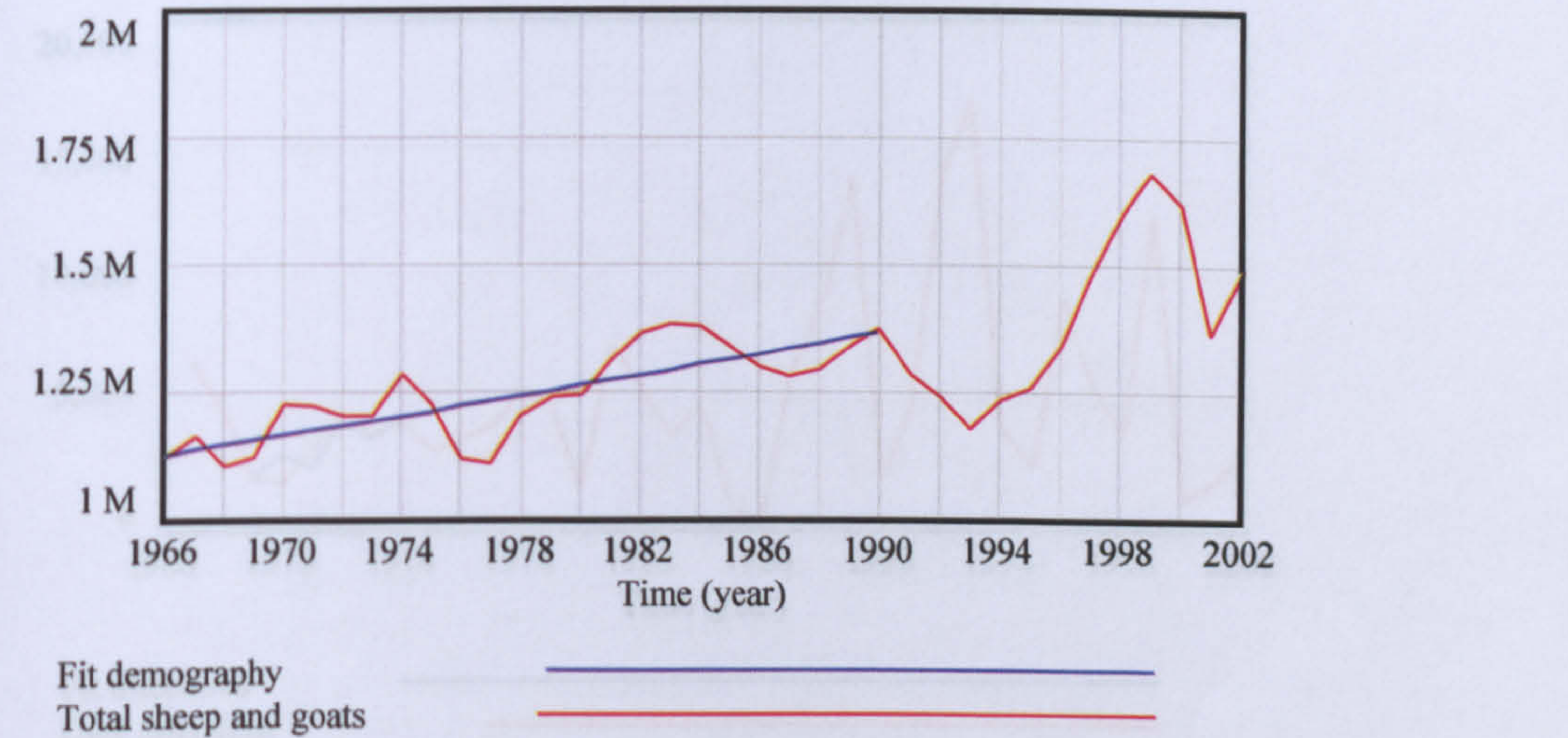
Hentiy Aimag, sheep and goats

Fit demography
Total sheep & goats

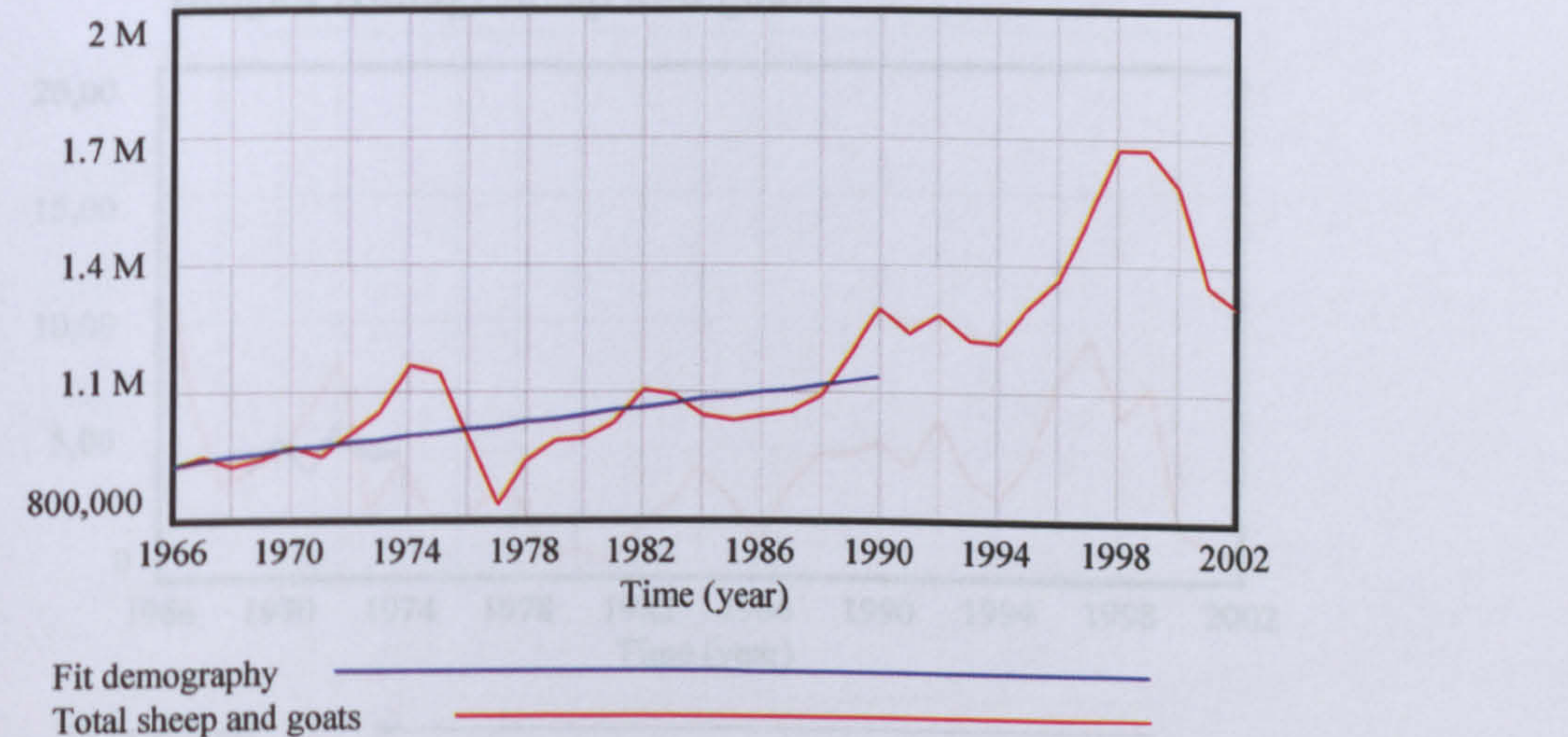
Suhbaatar Aimag, sheep and goats



Hovsgol Aimag, sheep and goats



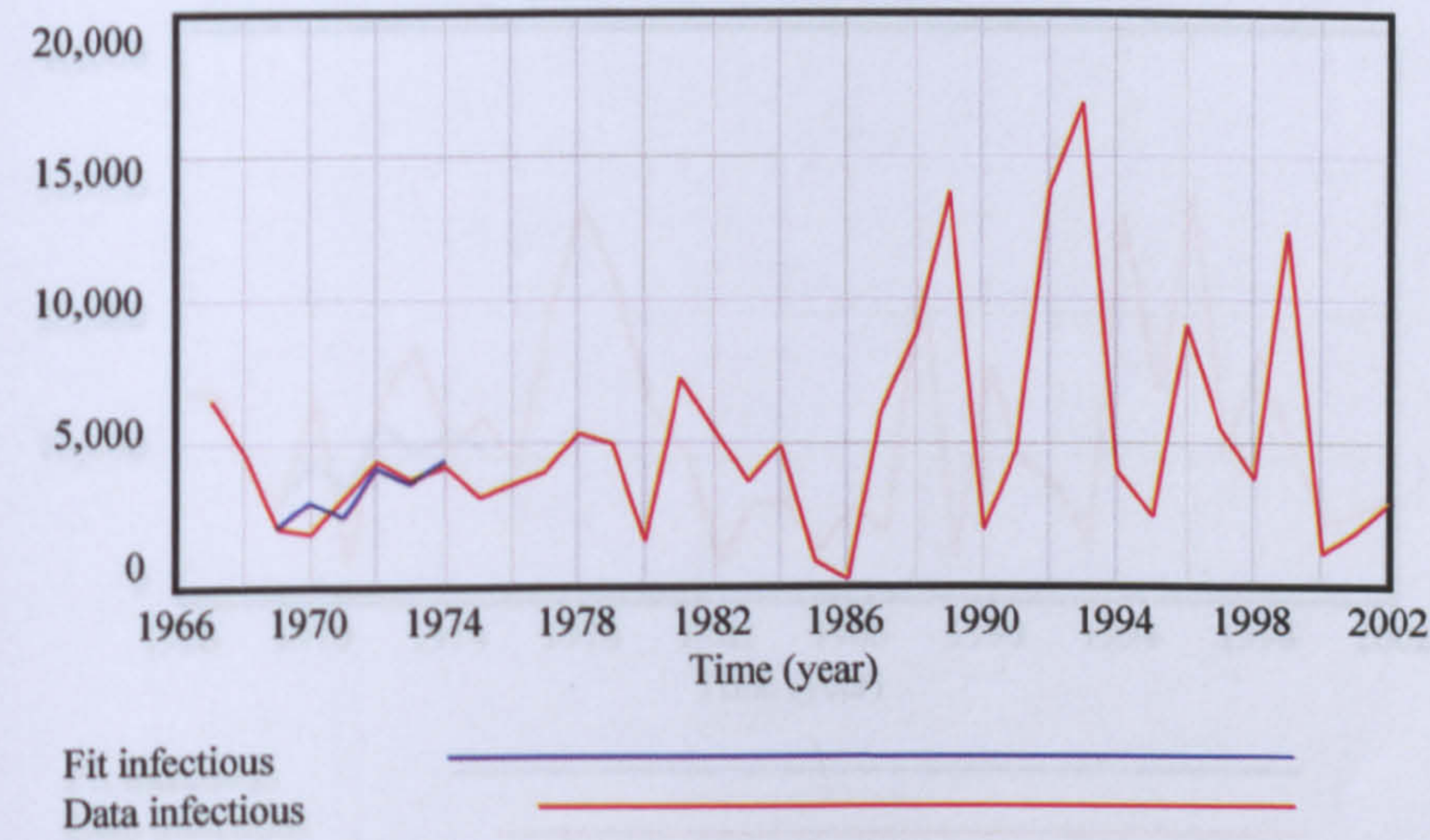
Tov Aimag, sheep and goats



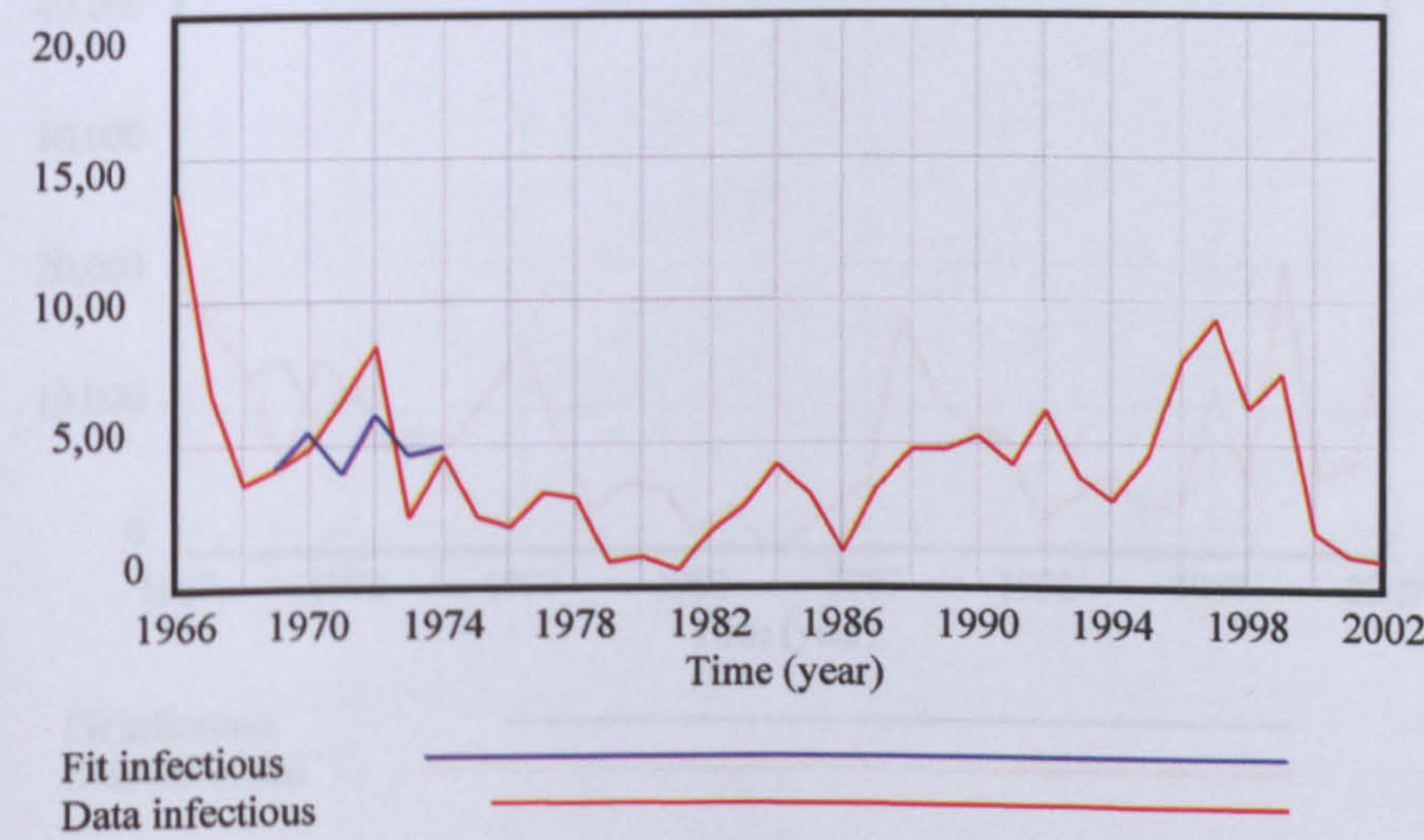
Appendix 6.3.: Mathematical fit of the transmission rate

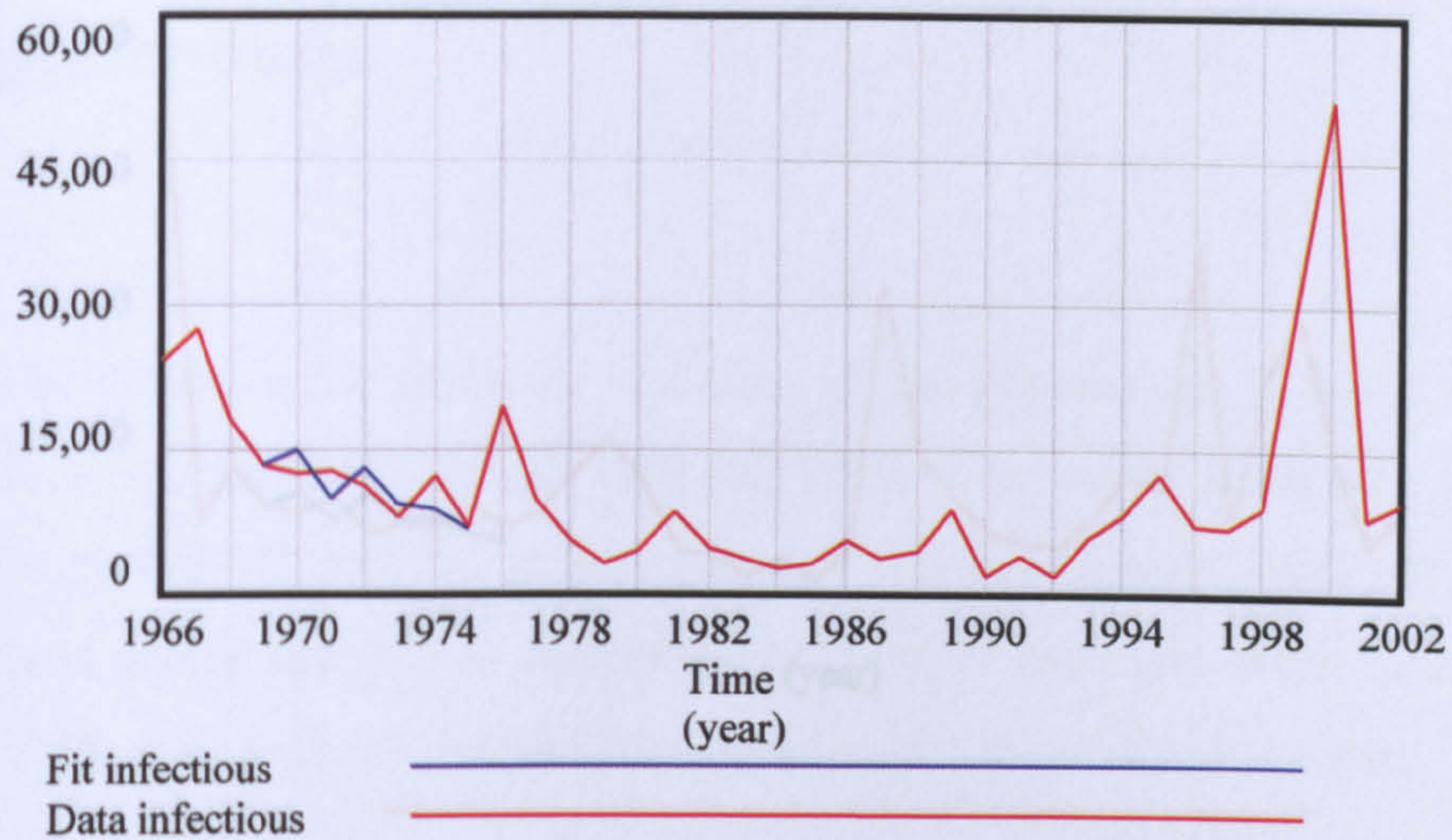
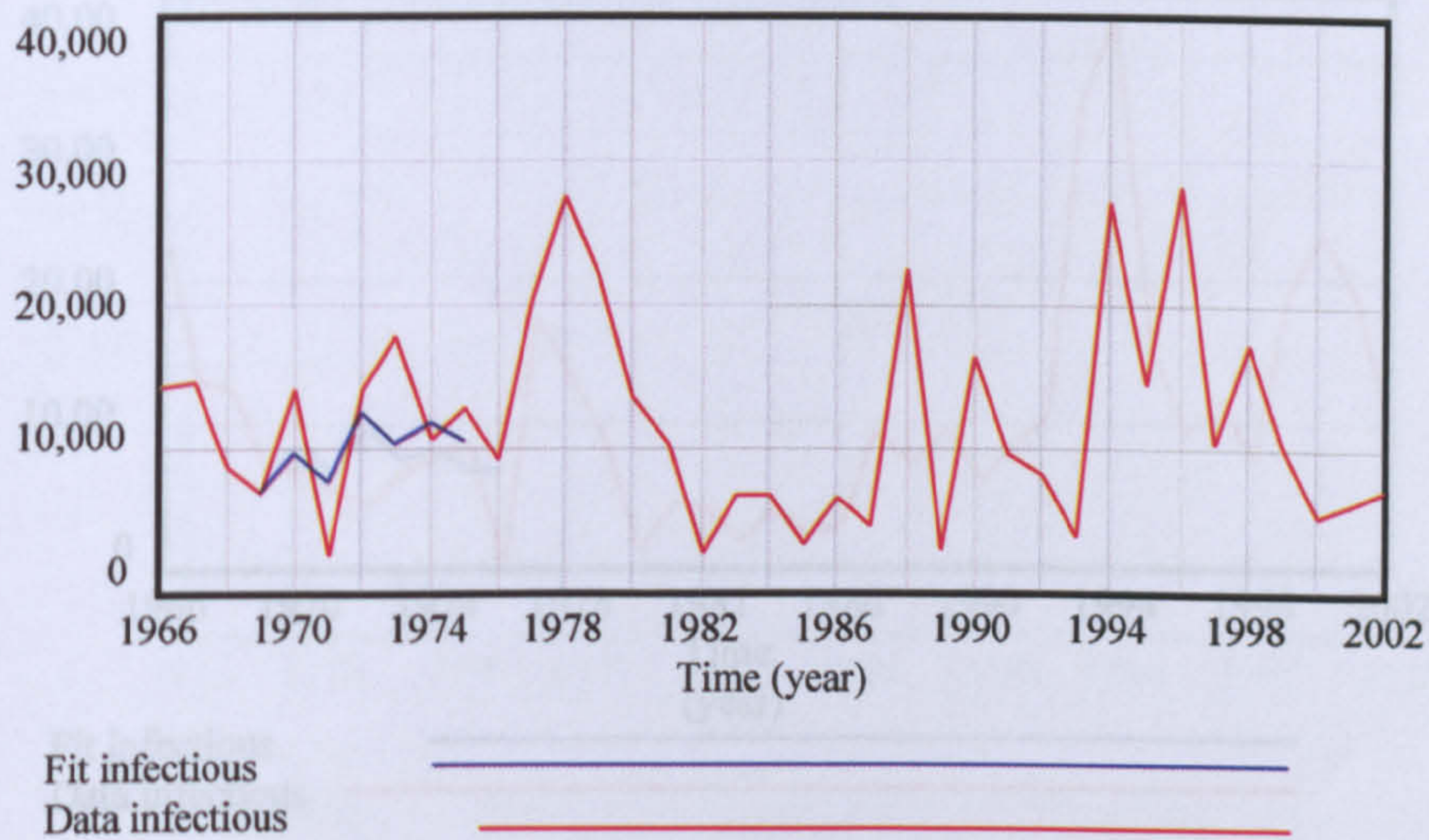
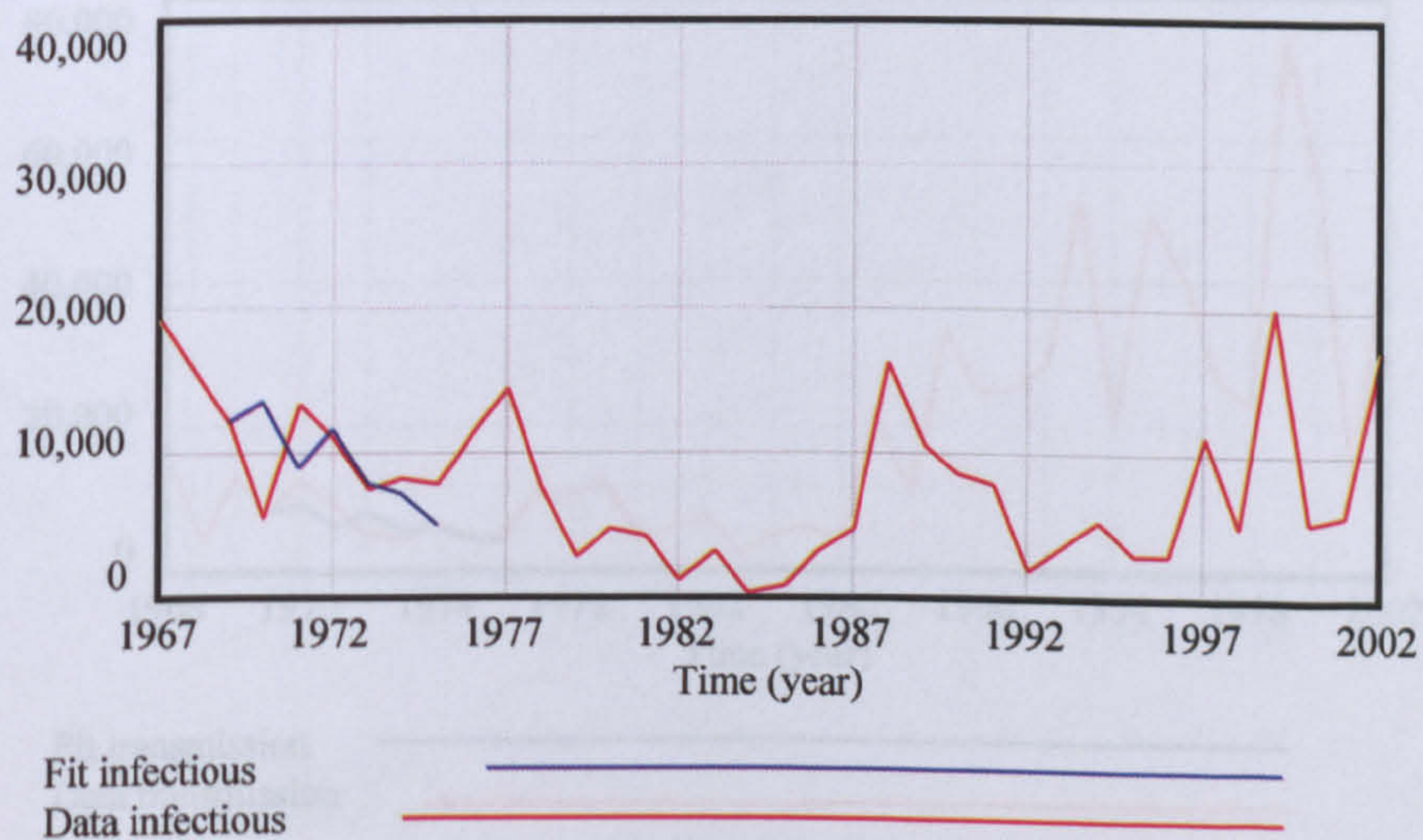
The transmission rate (β) was fitted to the data of the susceptible (S) and infected (I) small ruminants for the time period without disease control interventions, to best observe the natural spread of disease. The *test and slaughter* campaigns came to an end in 1968, and the whole herd vaccination campaign started gradually in 1975. The most likely range was defined with $0 \leq \text{animal contact rate} = 1.56e^{-7} \leq 0.1$ considering the previous work (Zinsstag J et al., 2005).

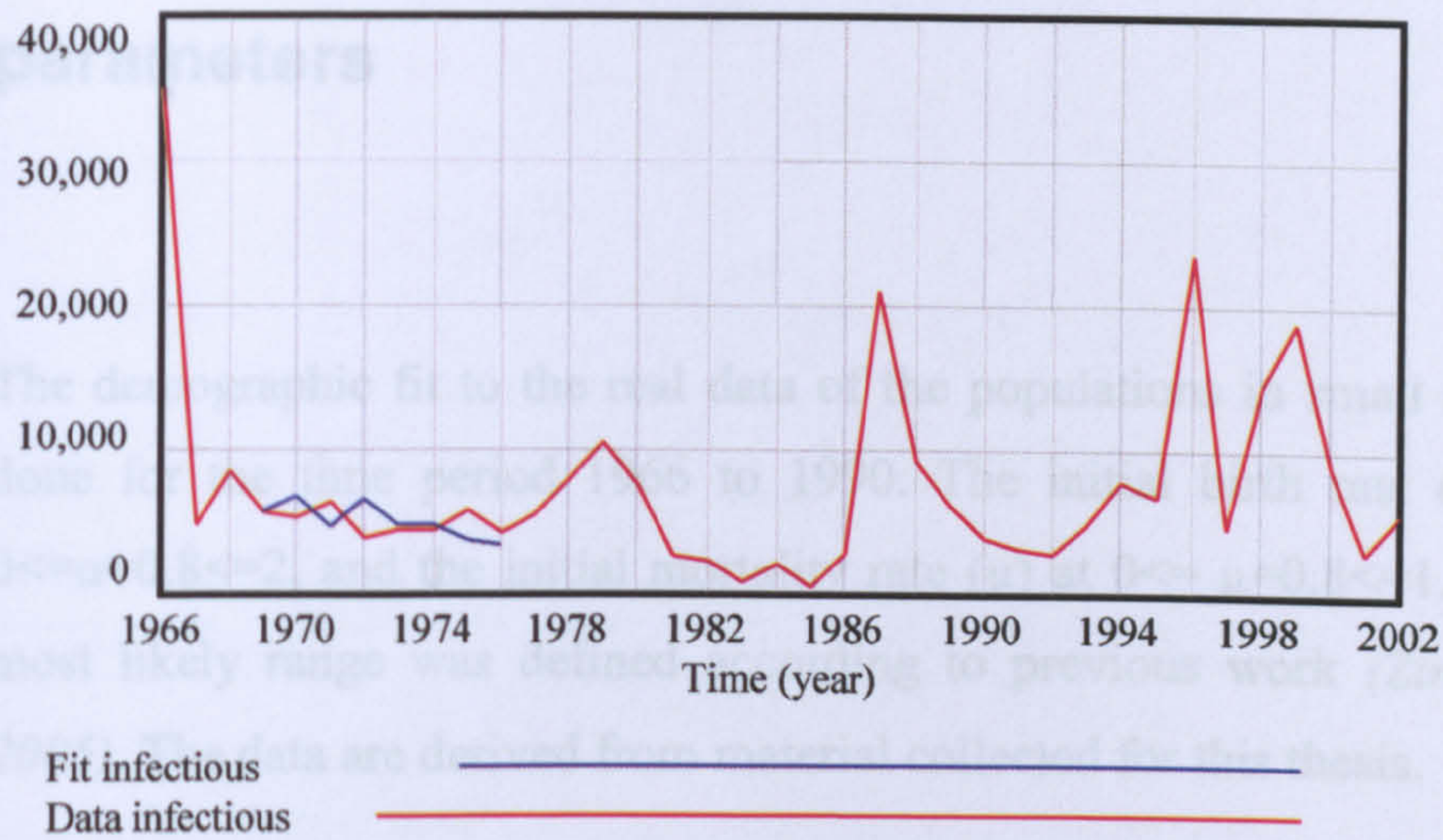
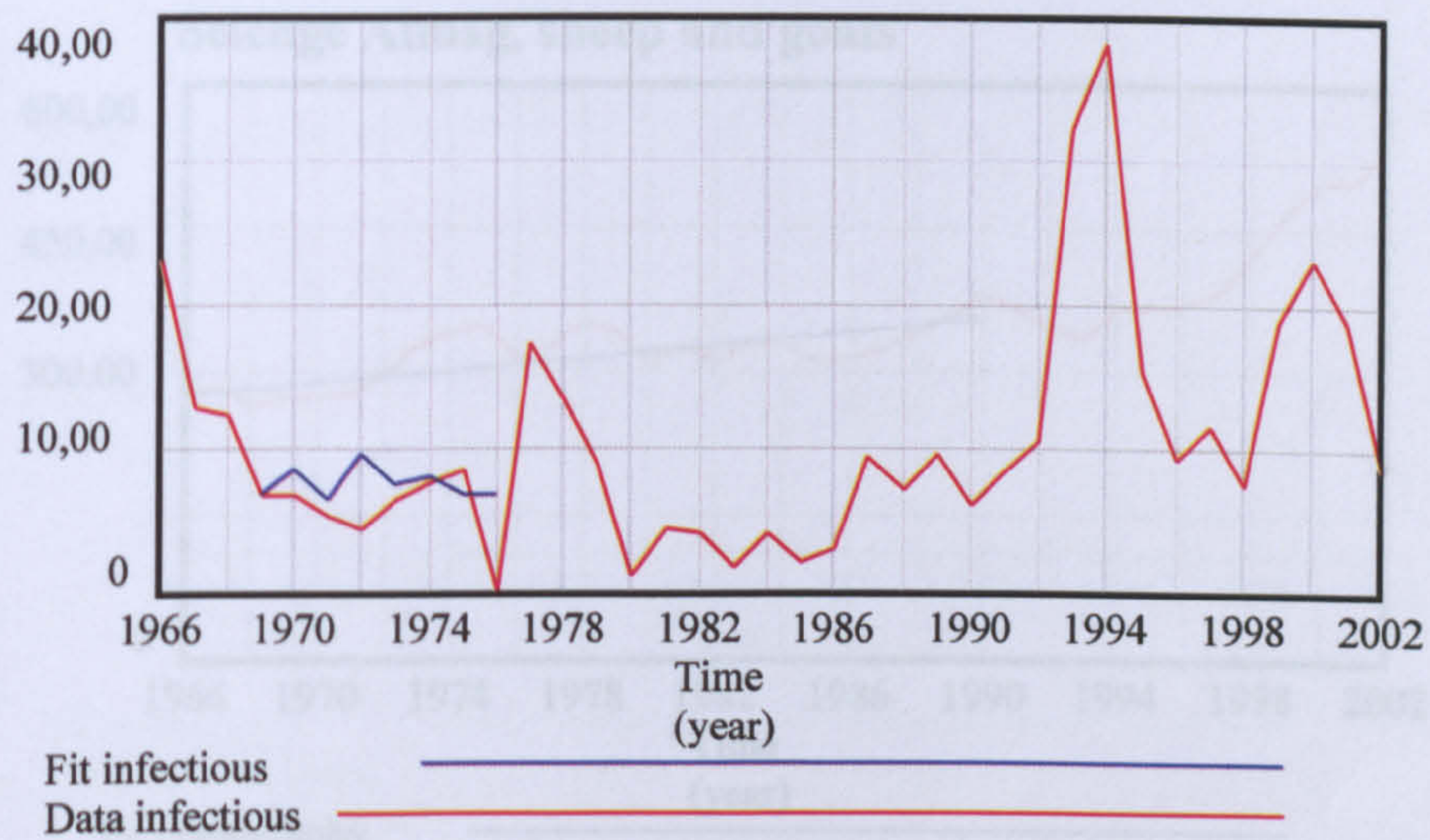
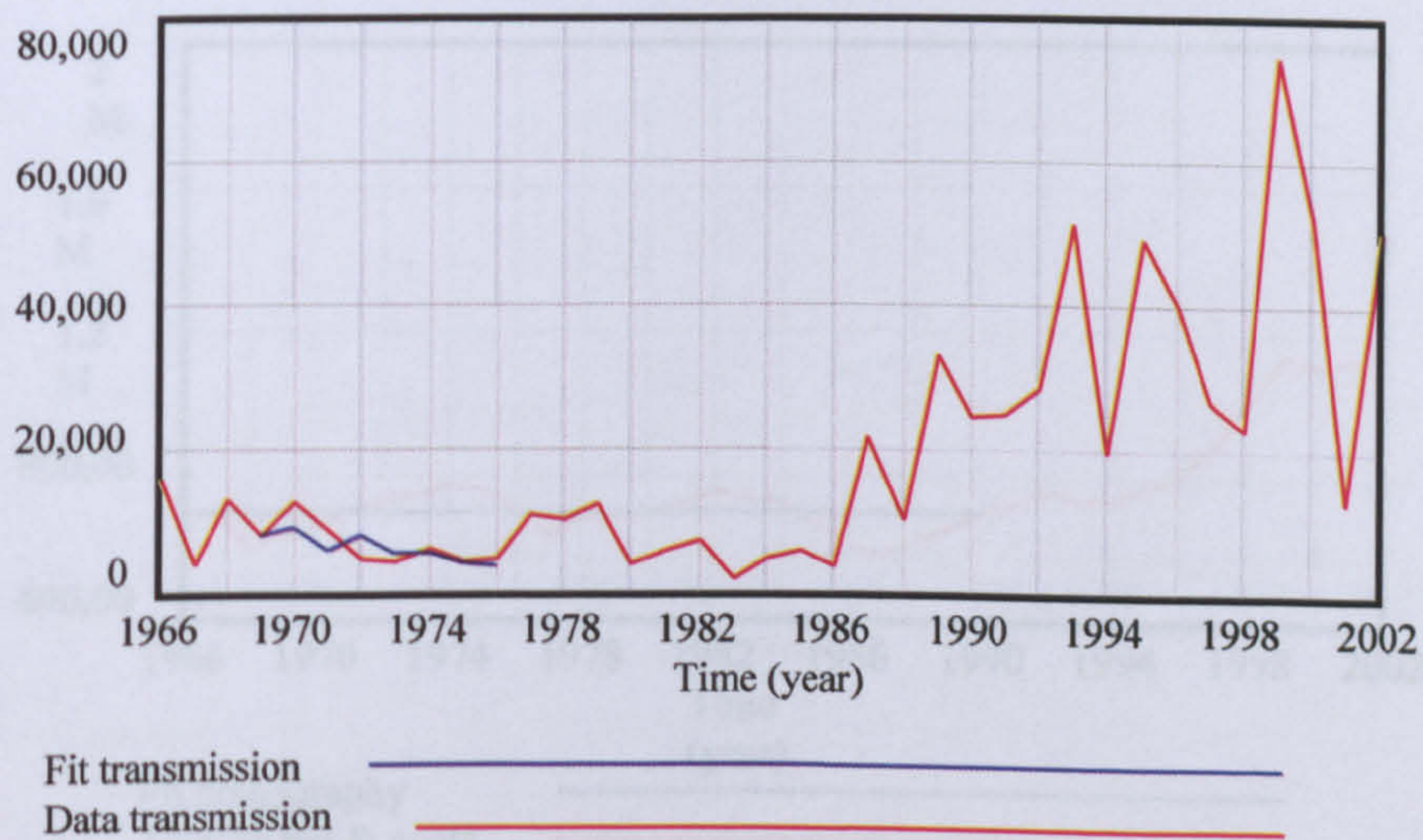
Selenge Aimag, sheep and goats



Bulgan Aimag, sheep and goats

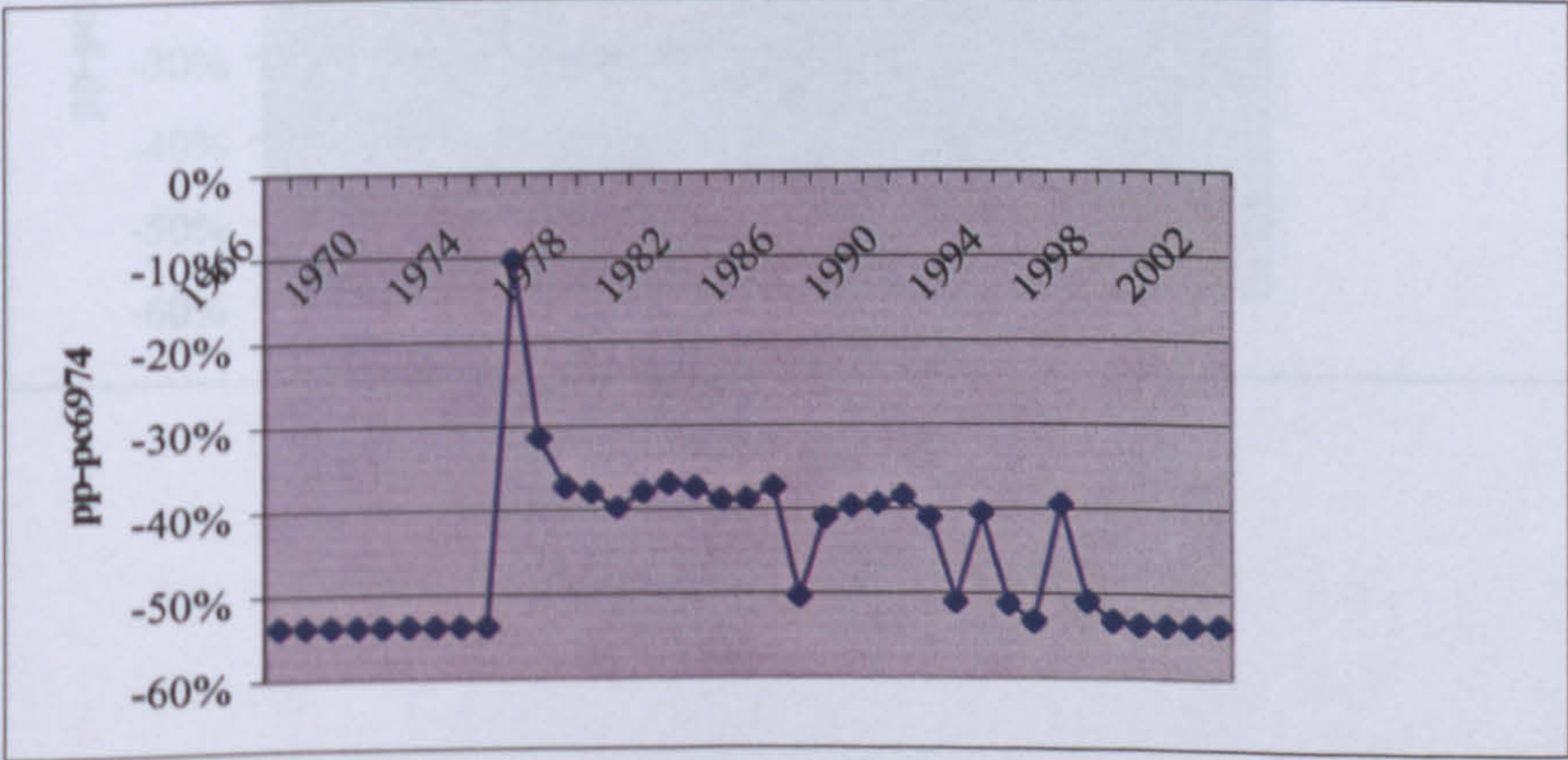
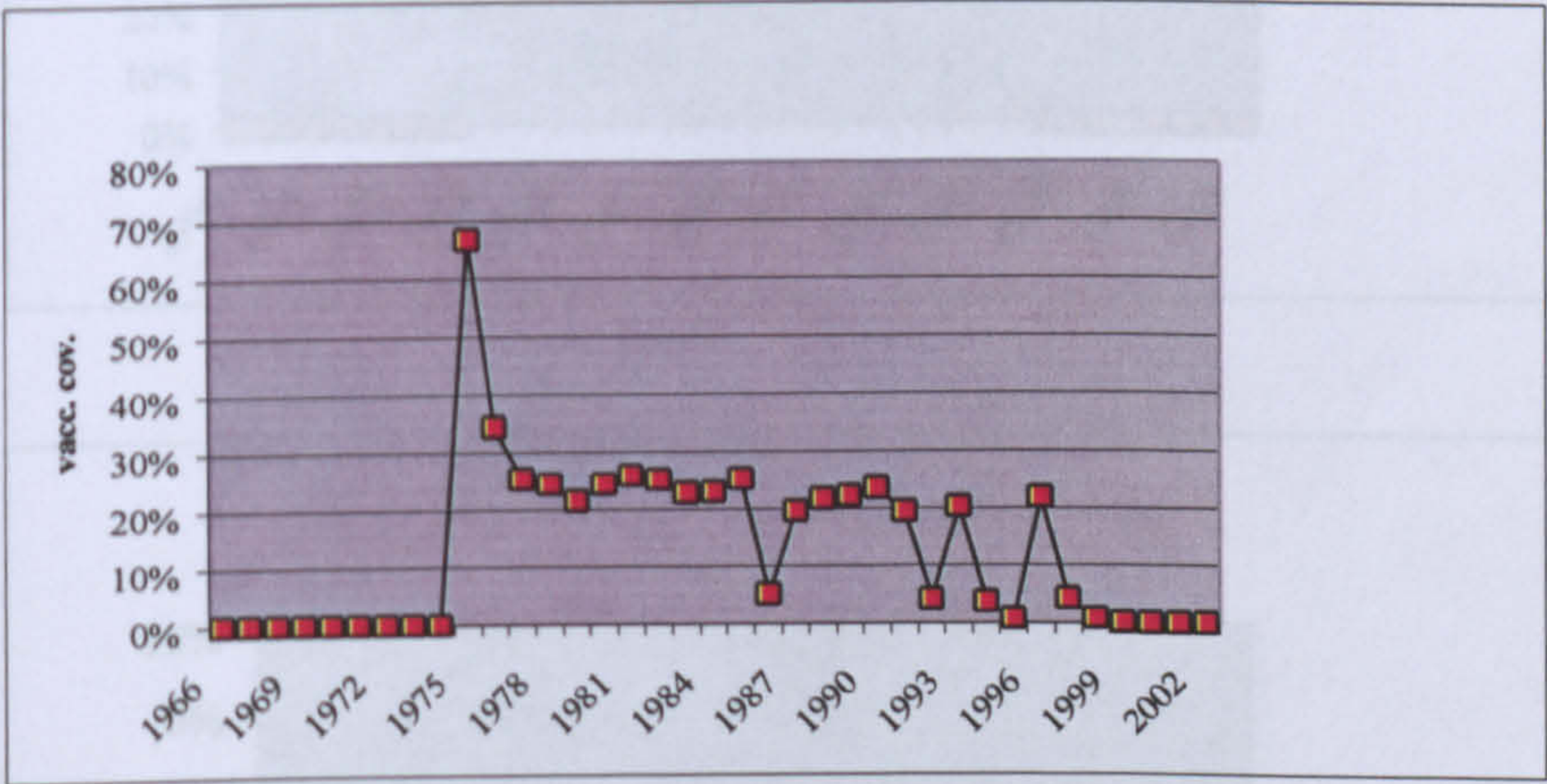
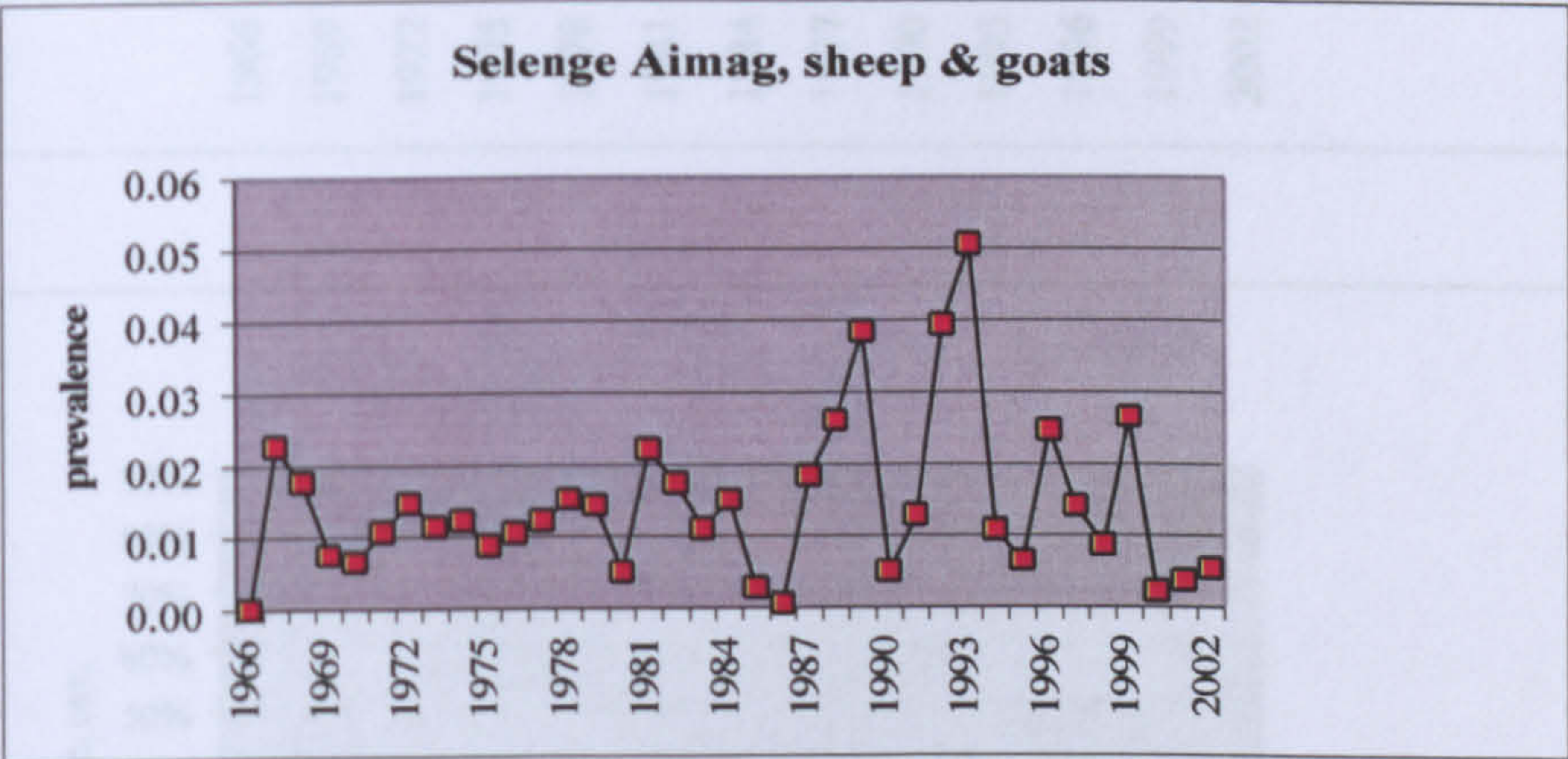


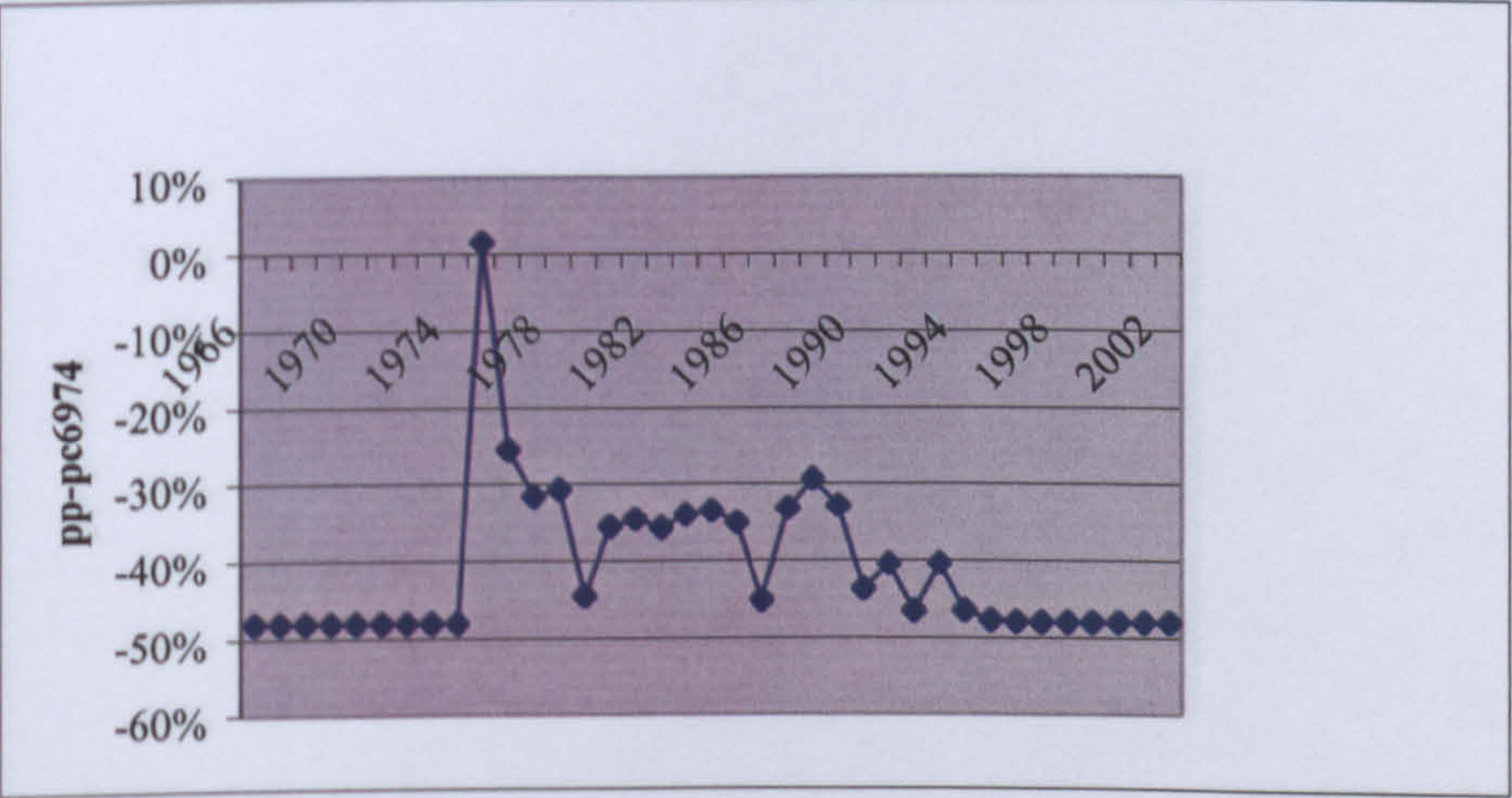
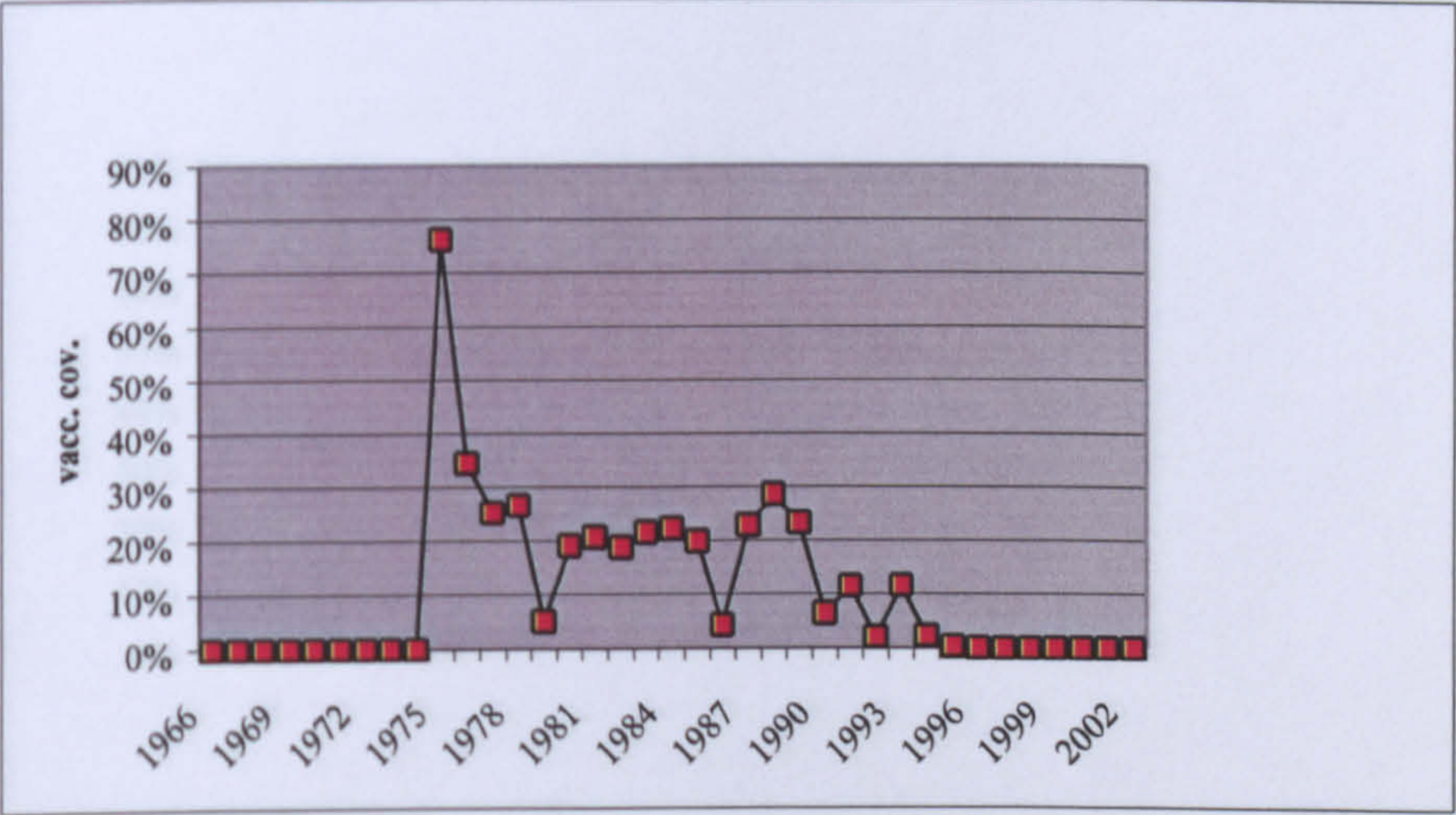
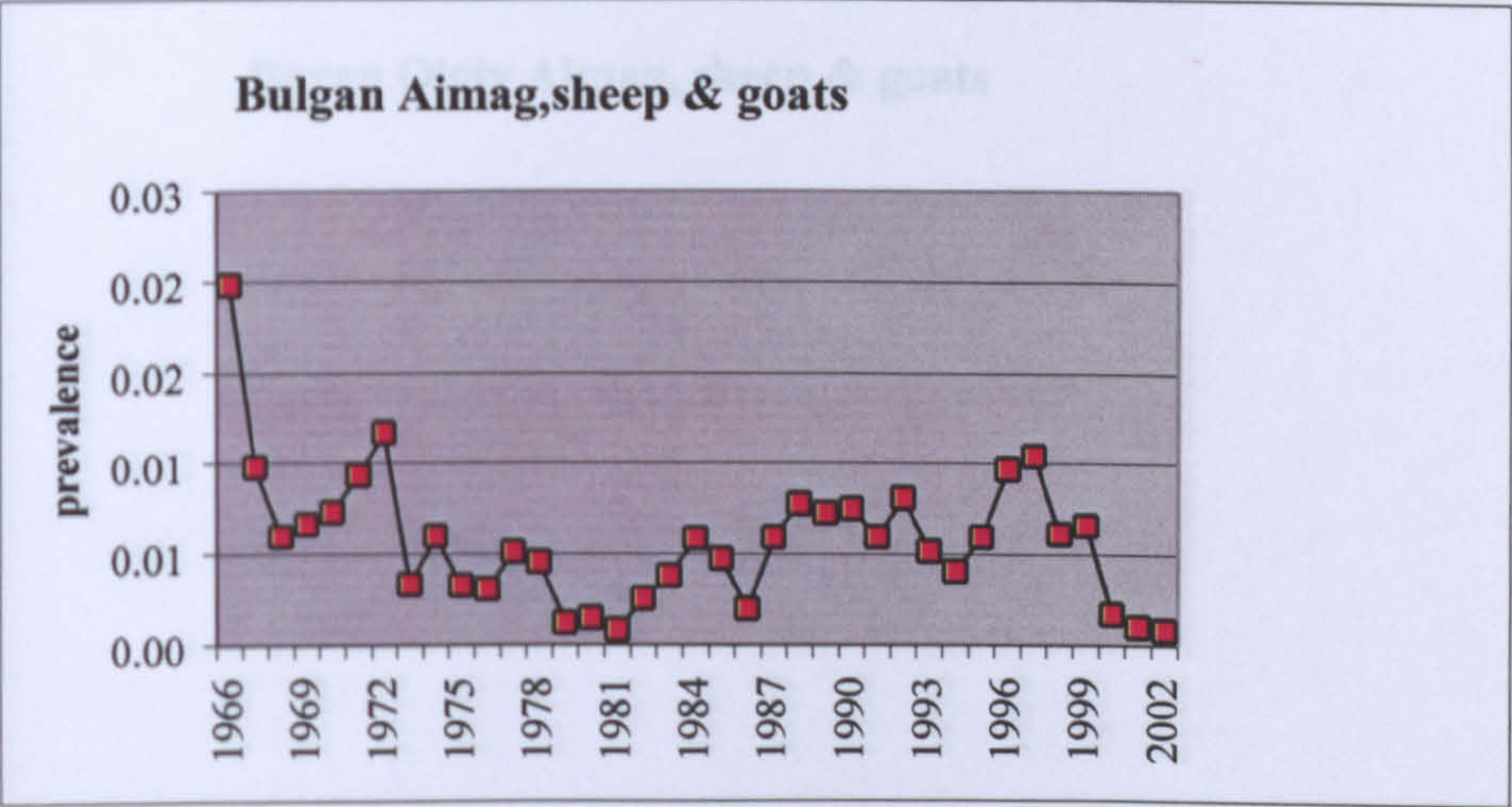
Bayan-Olgii Aimag, sheep and goats**Dornod Aimag, sheep and goats****Suhbaatar Aimag, sheep and goats**

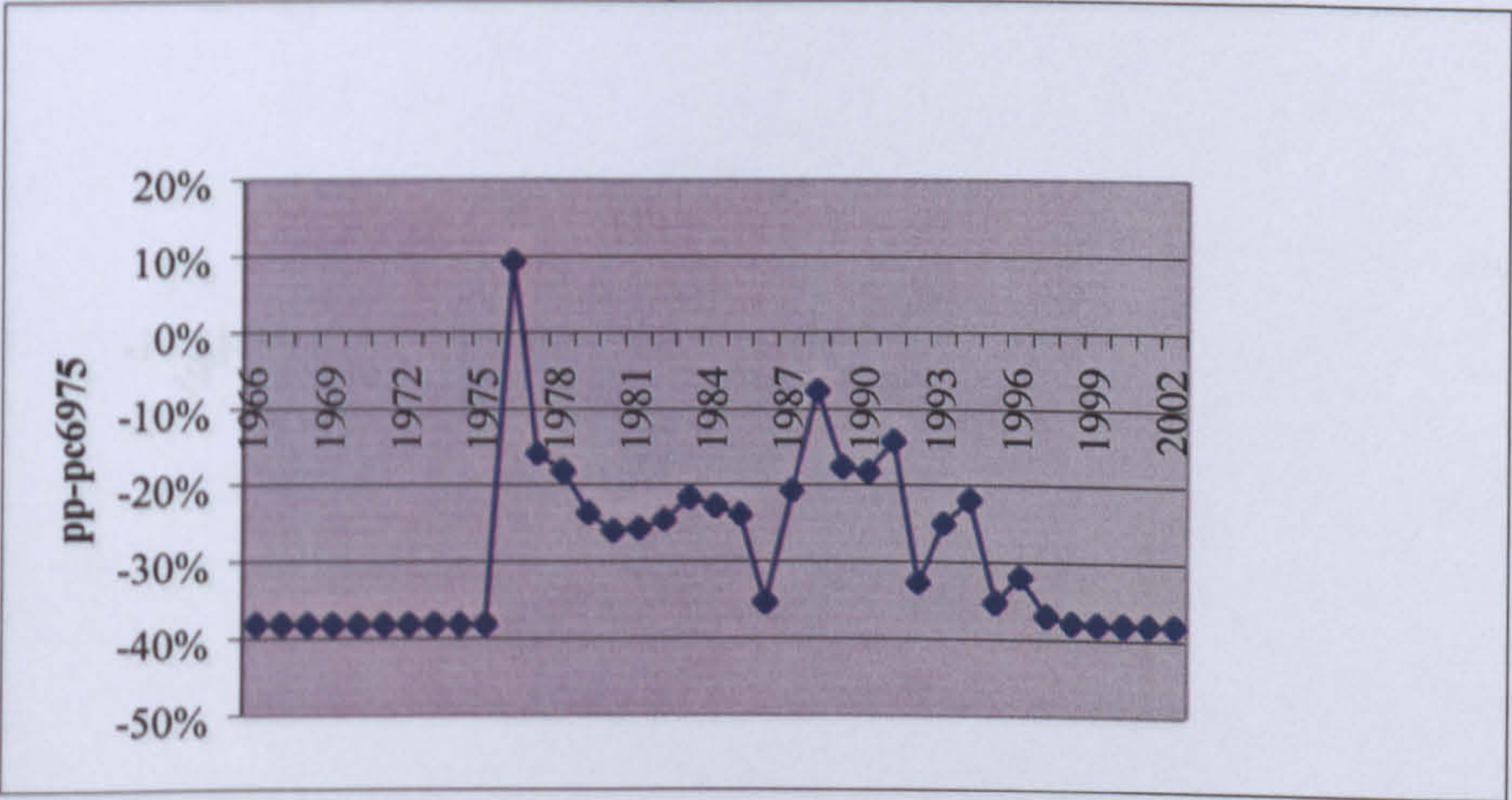
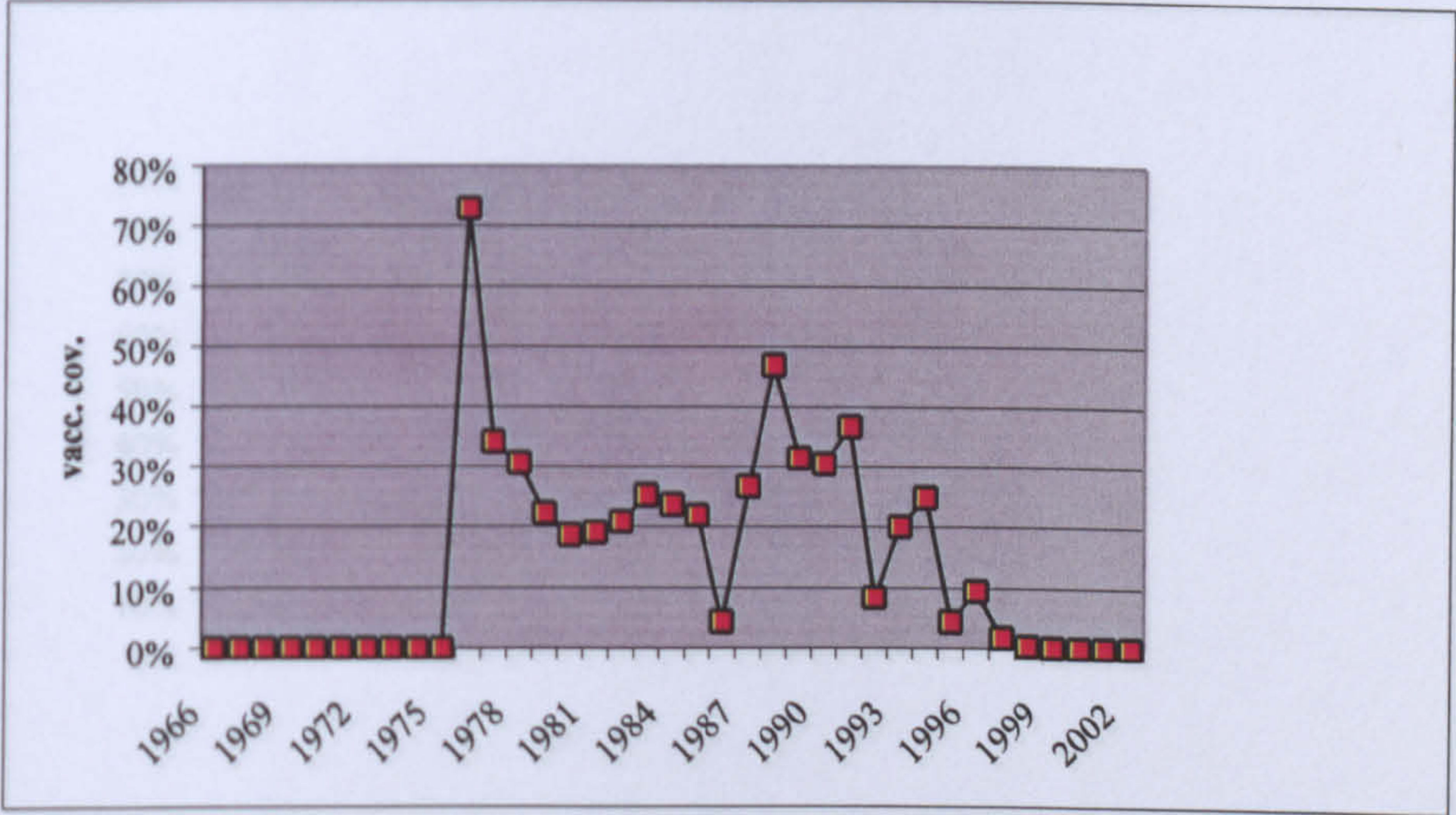
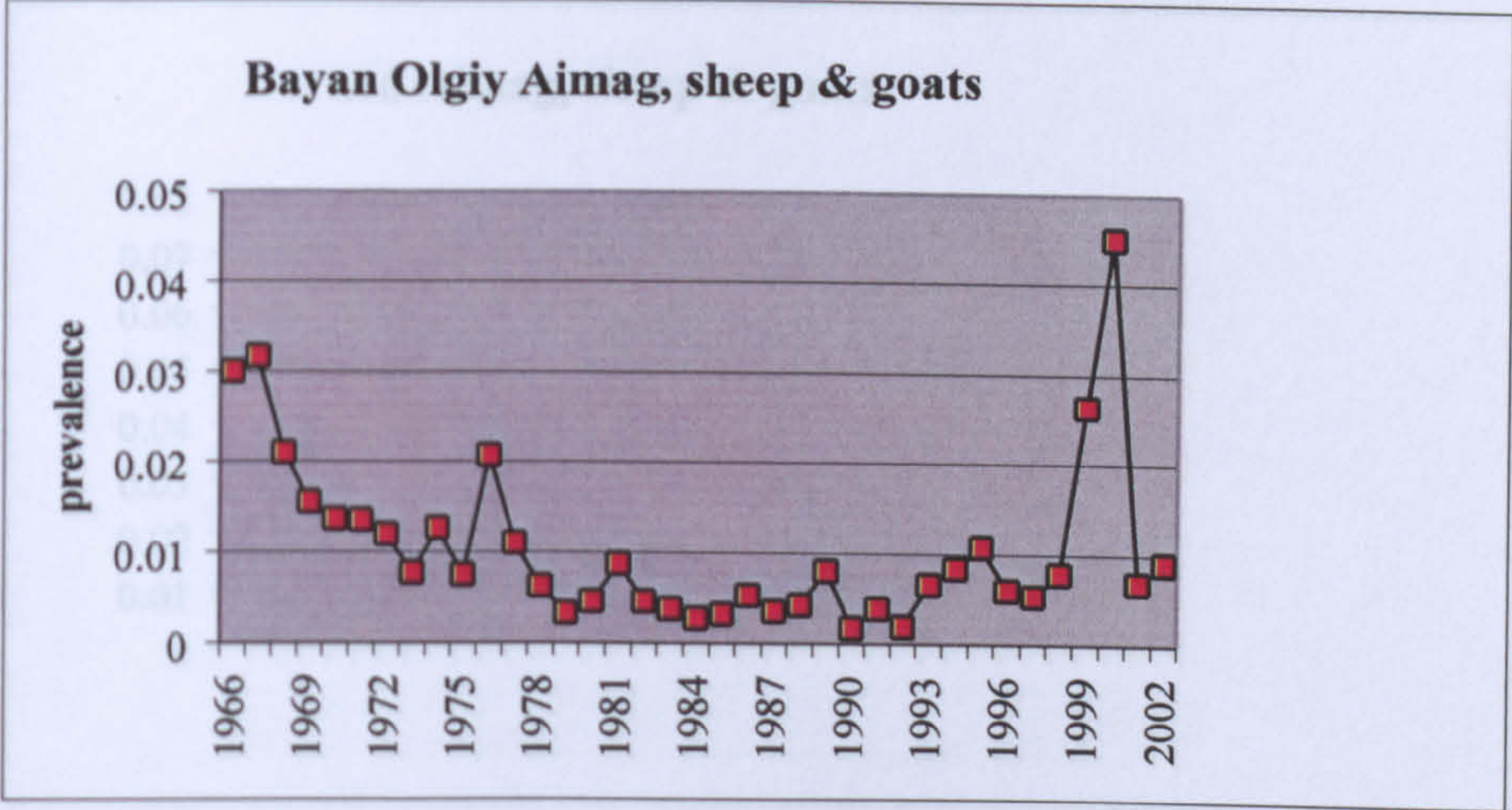
Hovsgol Aimag, sheep and goats**Hentiy Aimag, sheep and goats****Tov Aimag, sheep and goats**

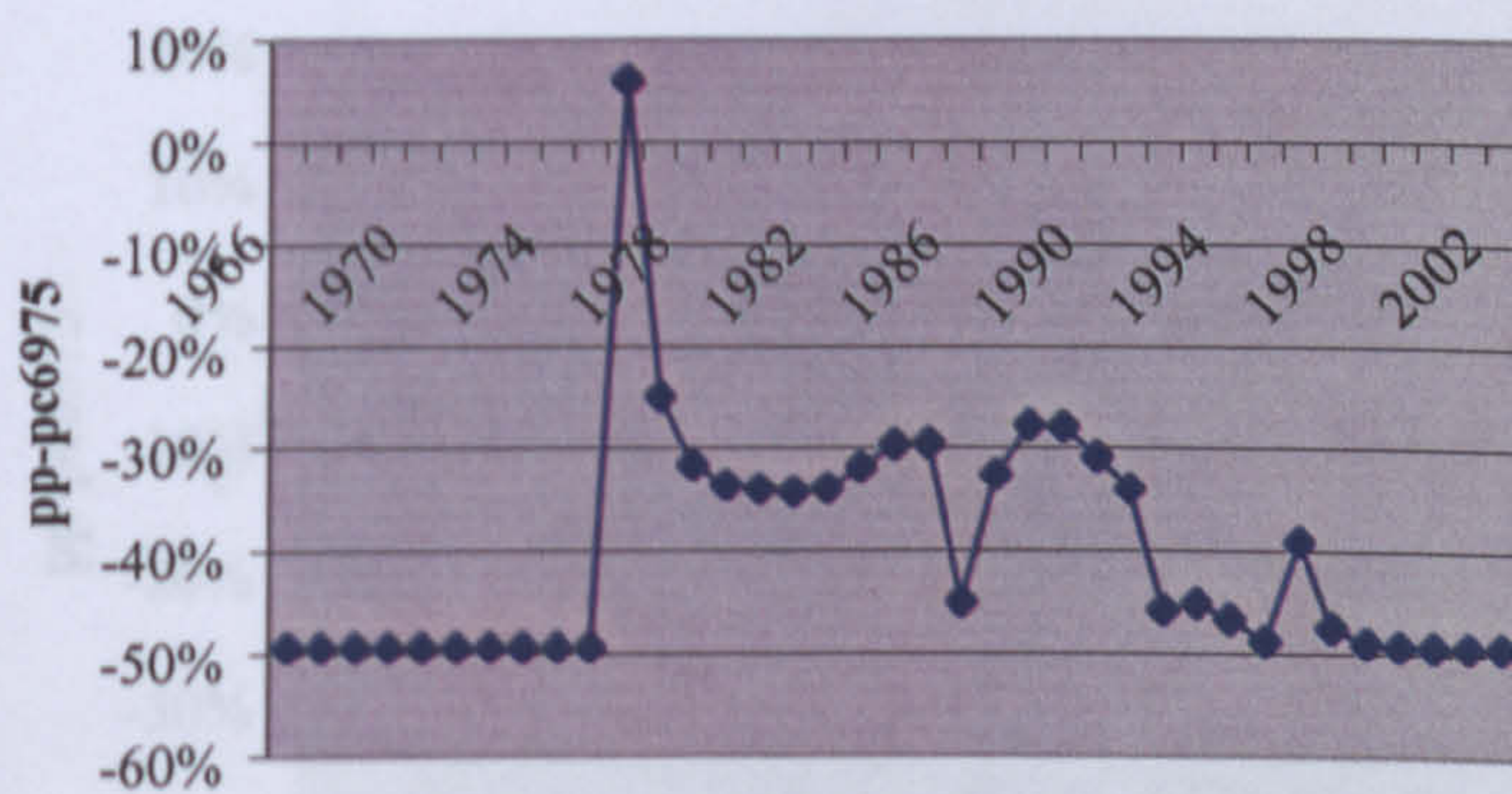
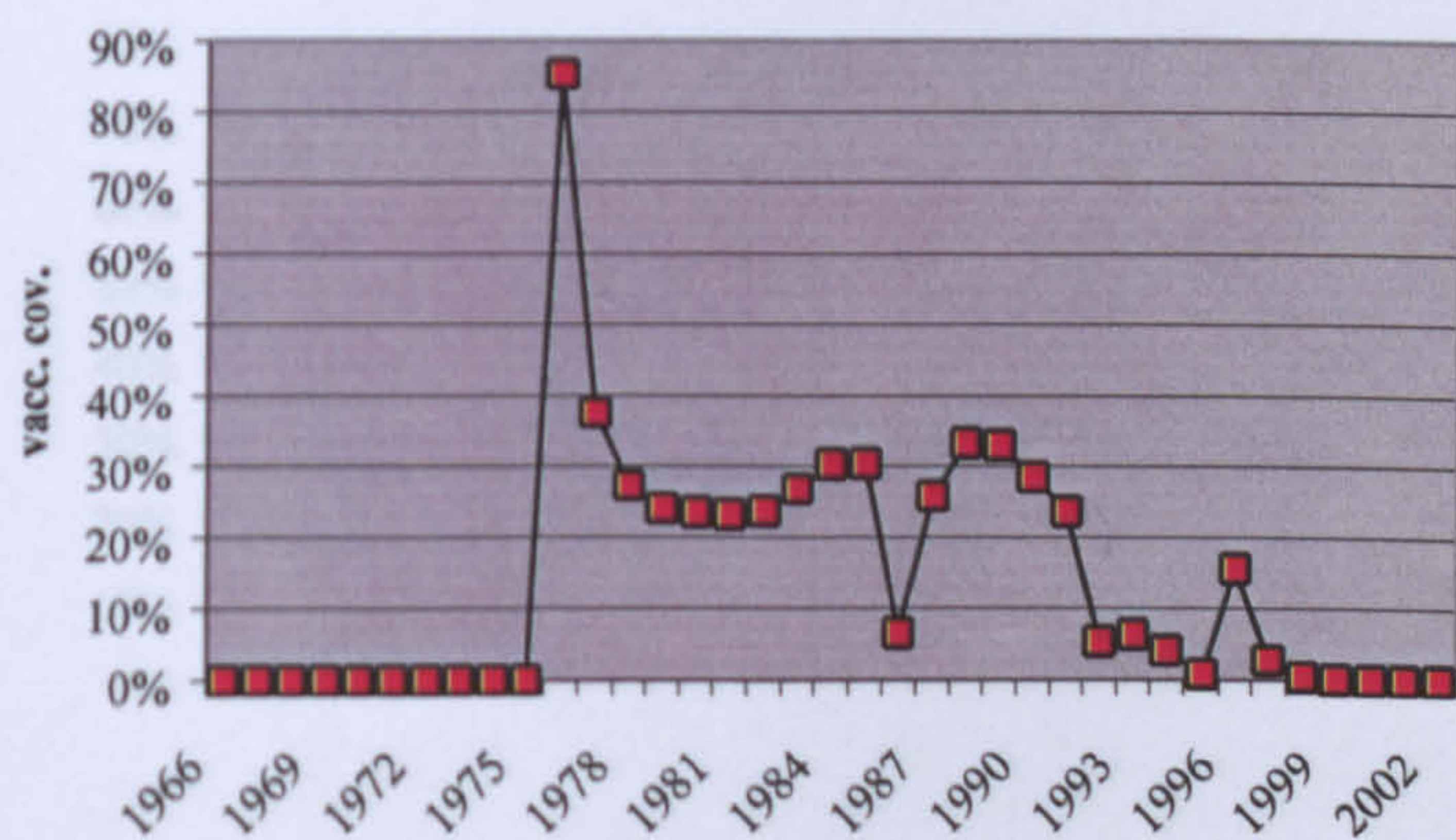
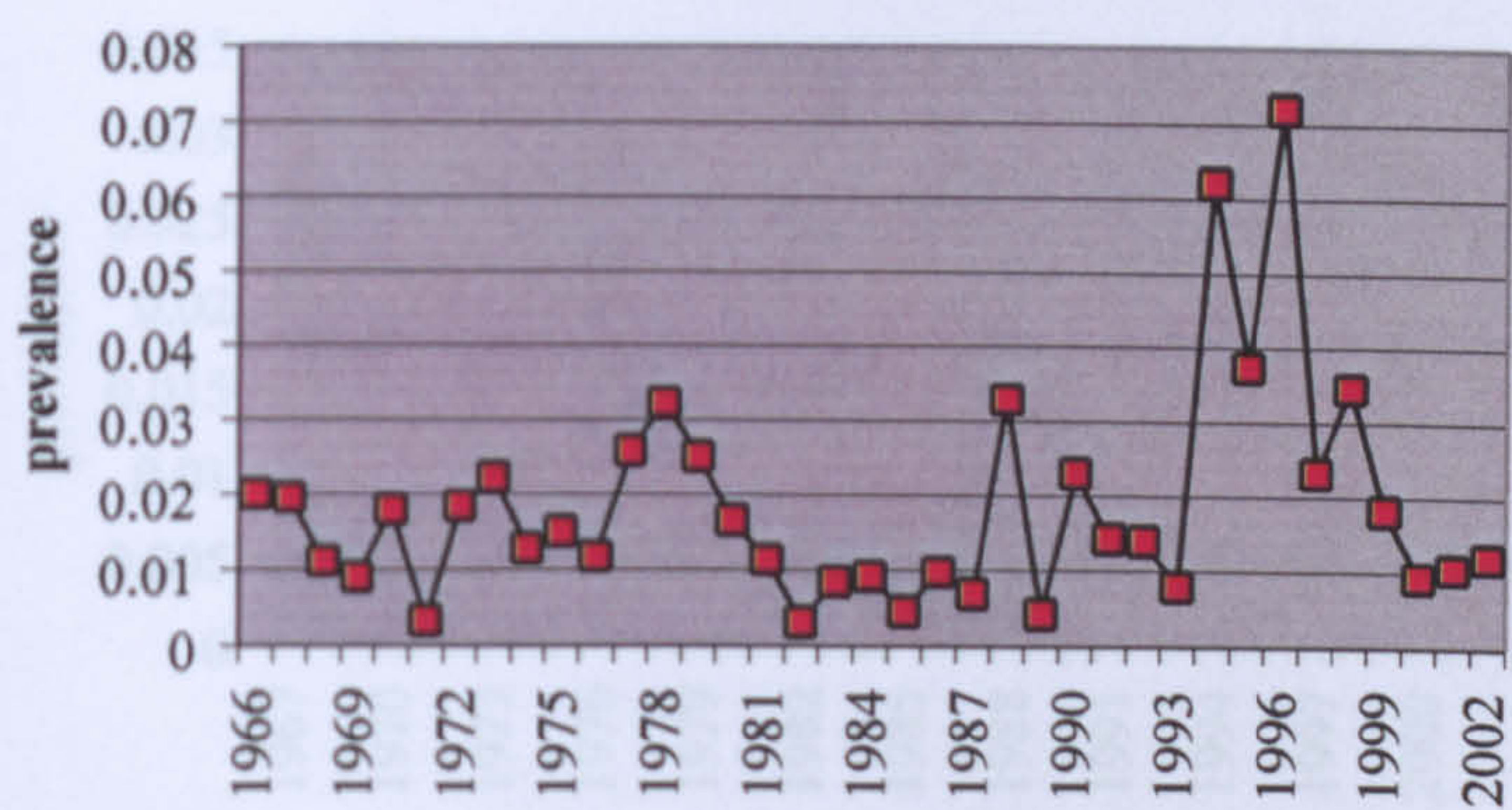
Appendix 6.4.: Discrepancy of vaccination from required vaccination level in small ruminants

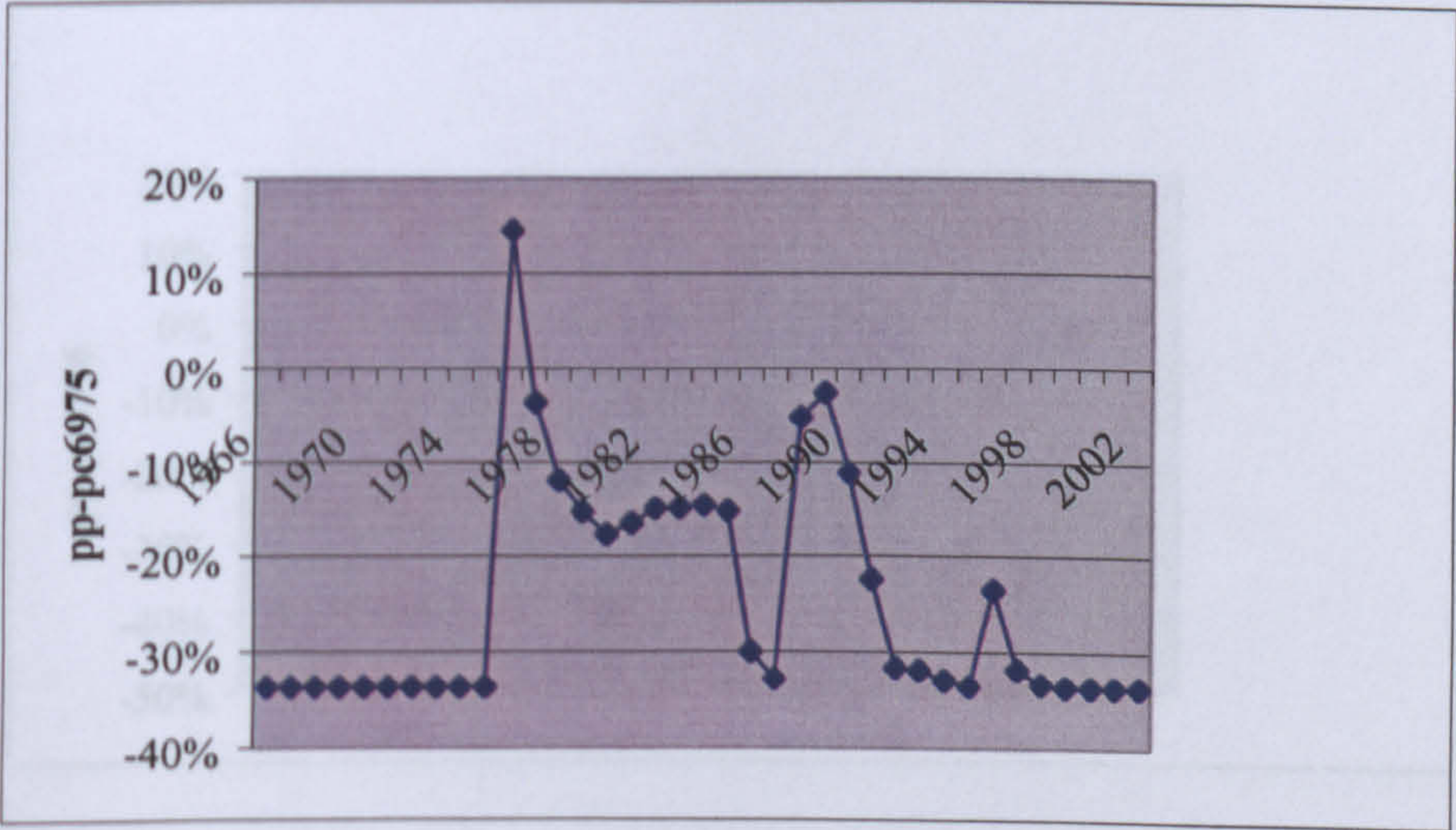
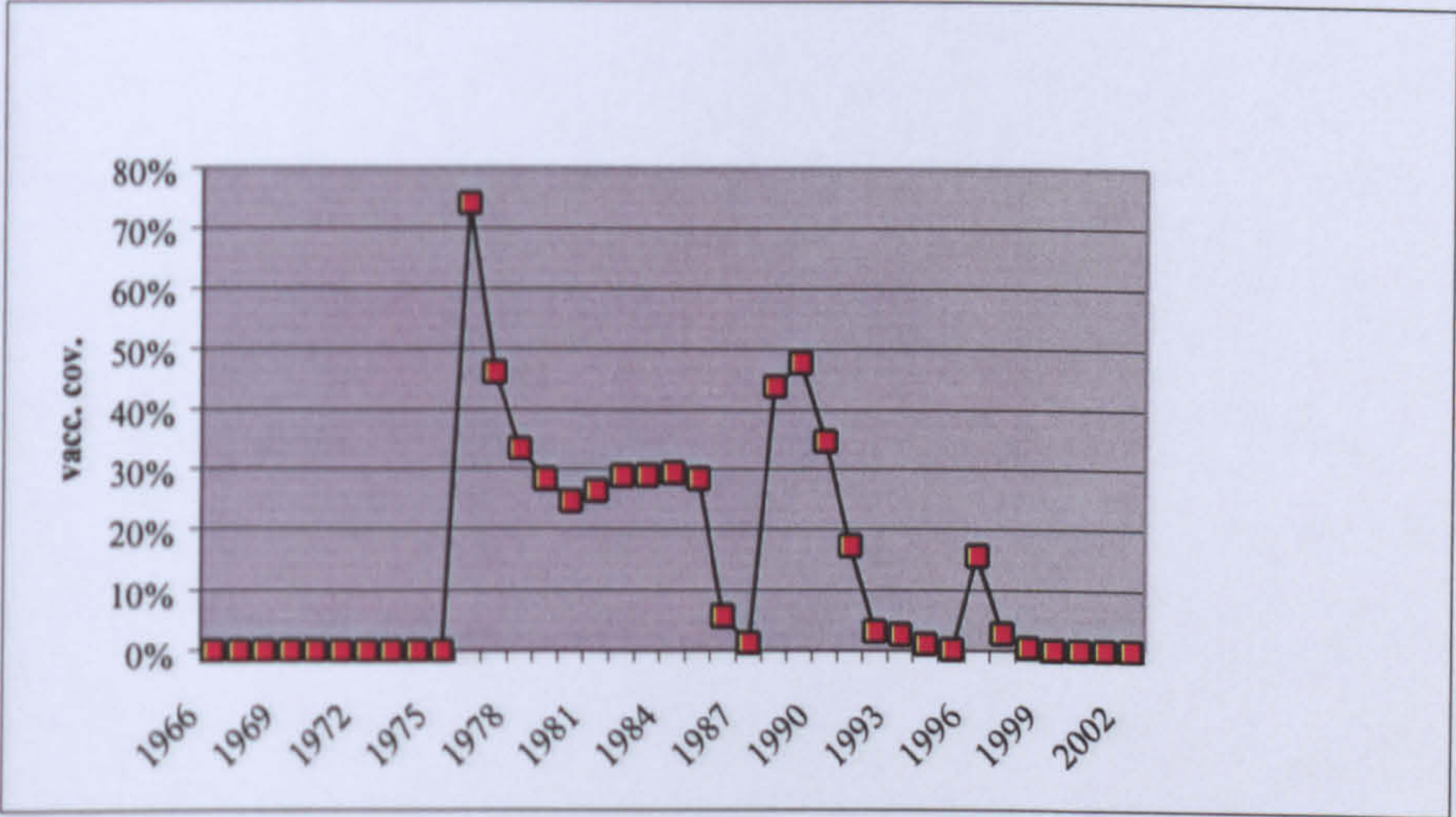
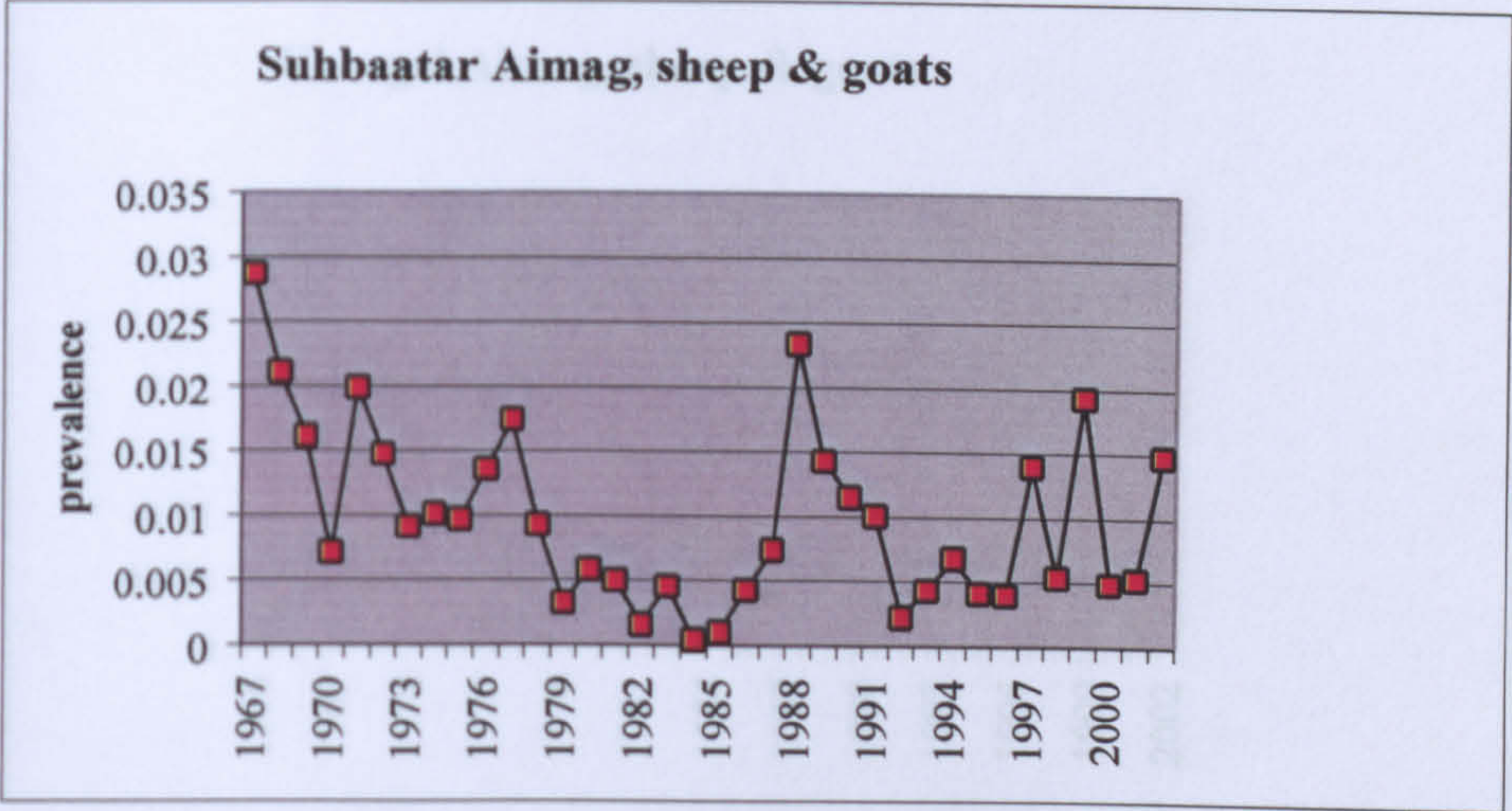
The local epidemiological situation is compared with the vaccination policy and gives the hint on the appropriateness of the chosen vaccination policy, by showing the discrepancy of the vaccination level from the required vaccination level (see chapter 6). The data are derived from material collected for this thesis.

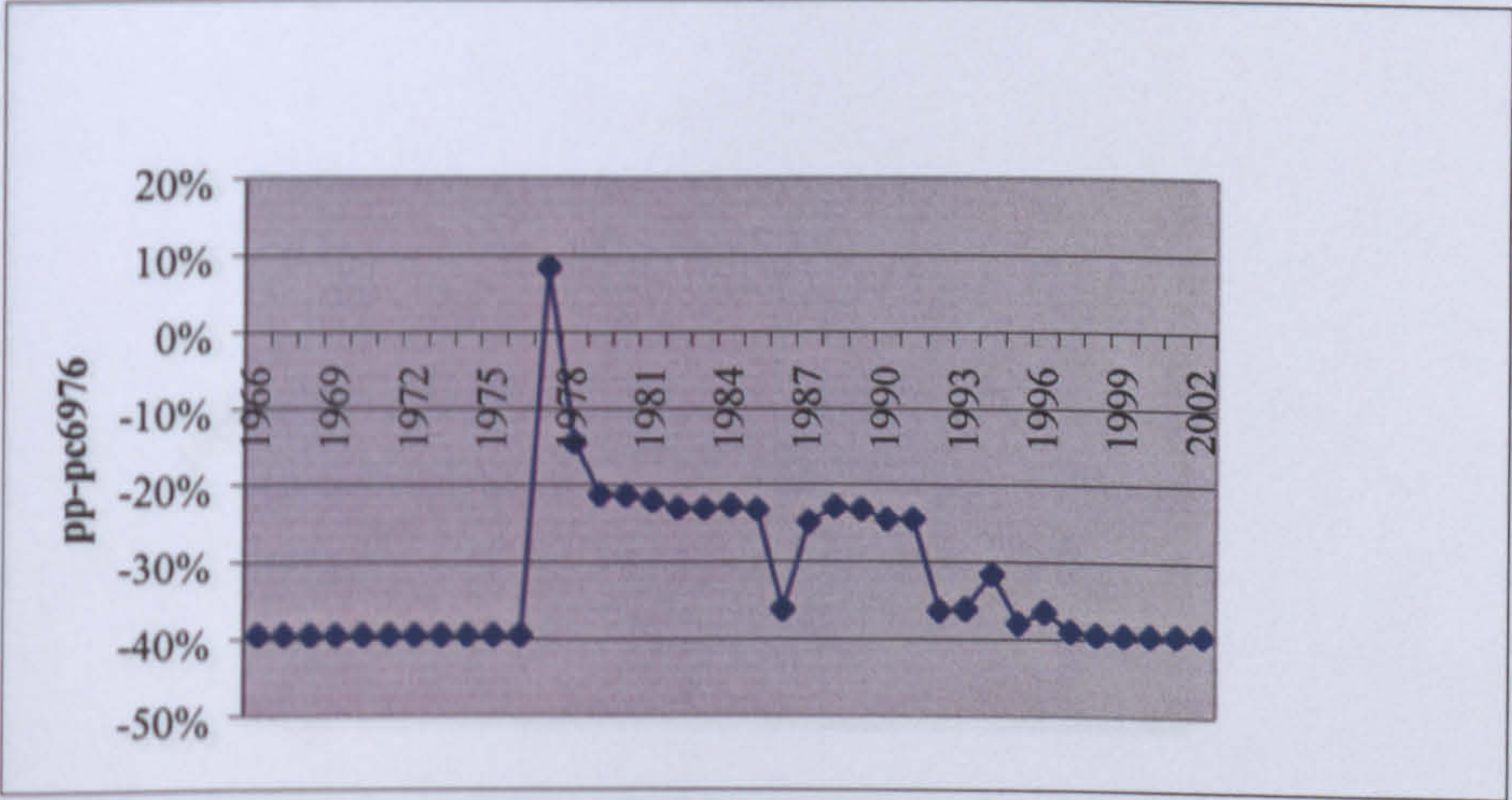
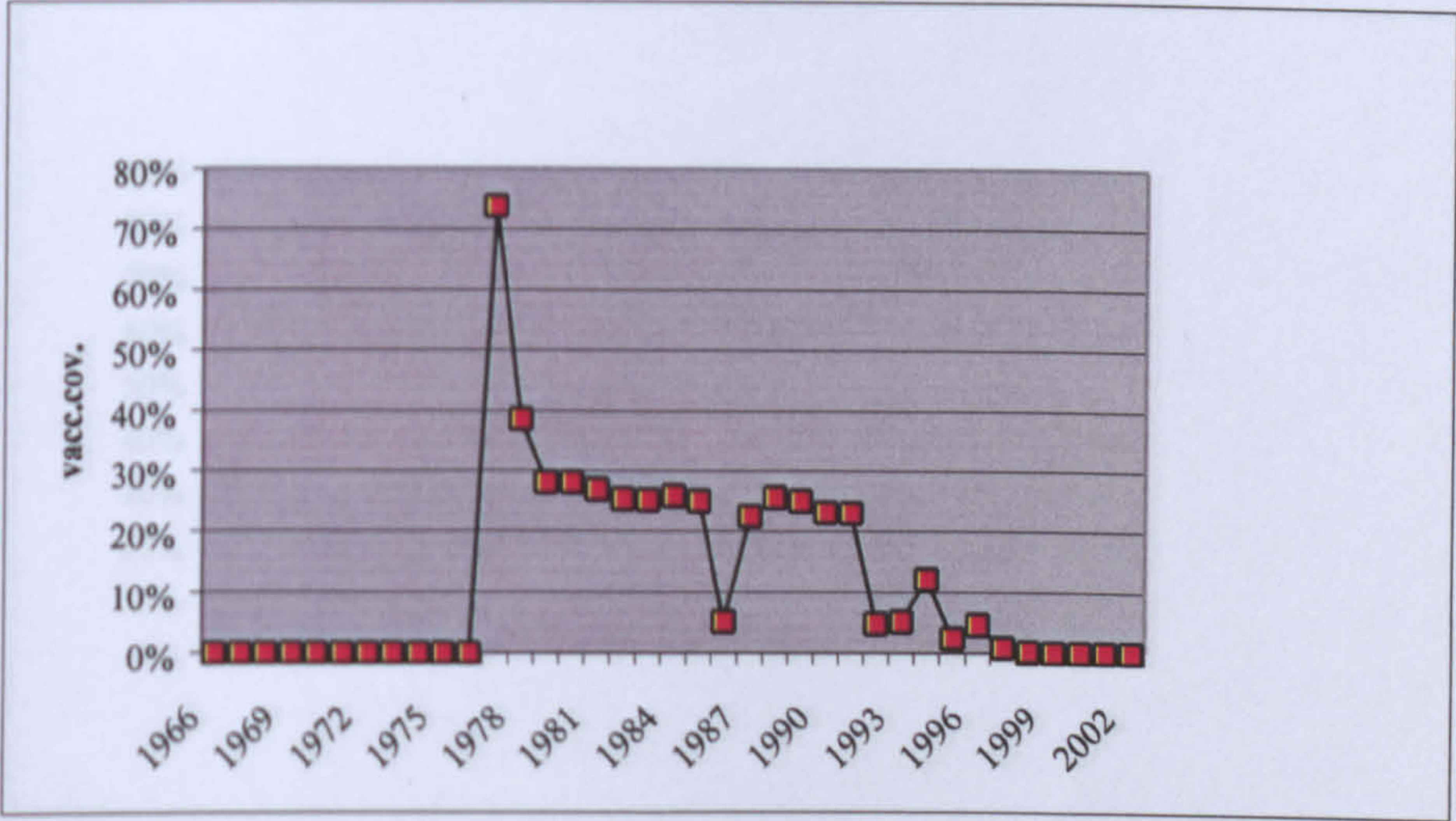
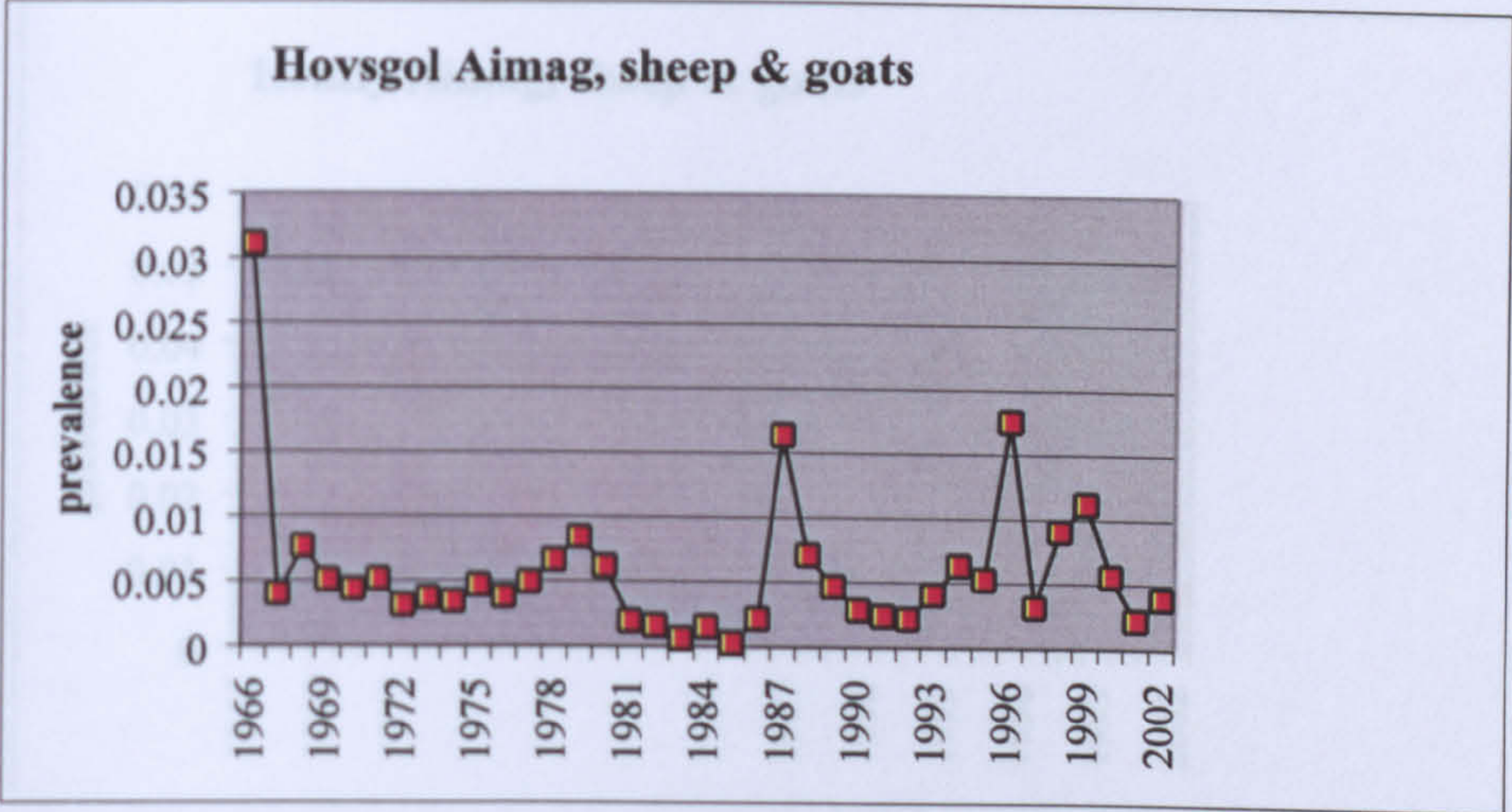


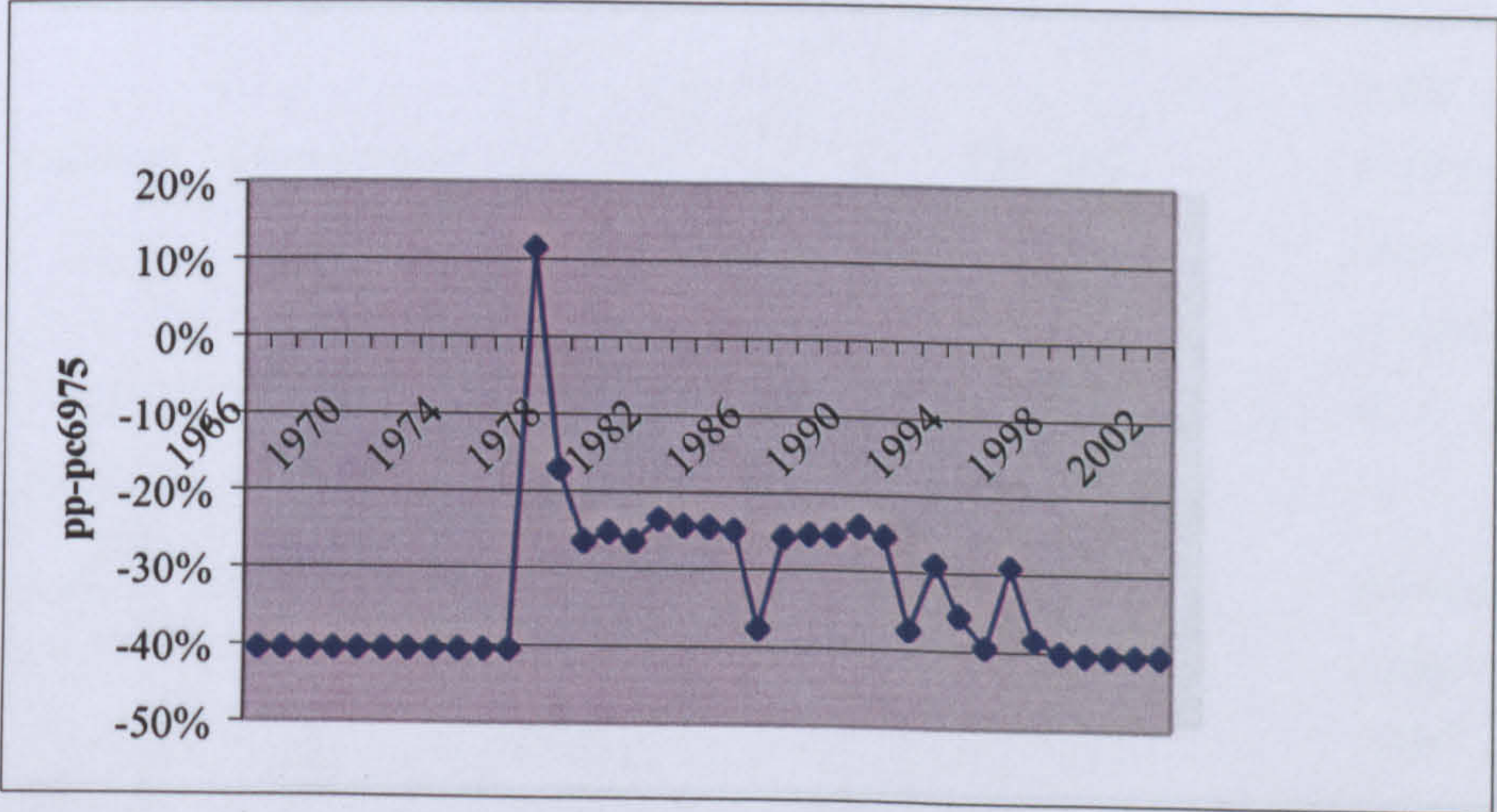
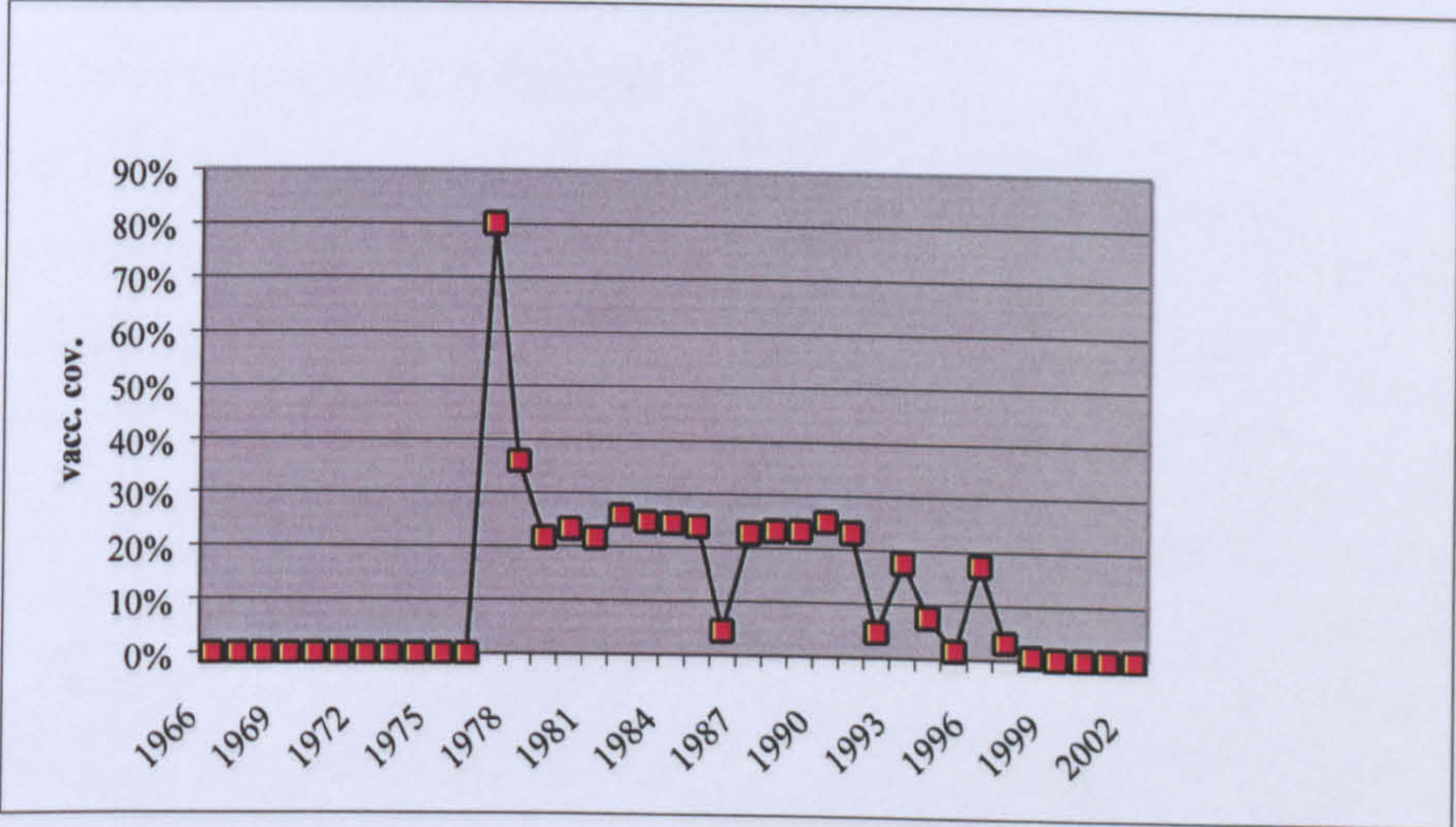
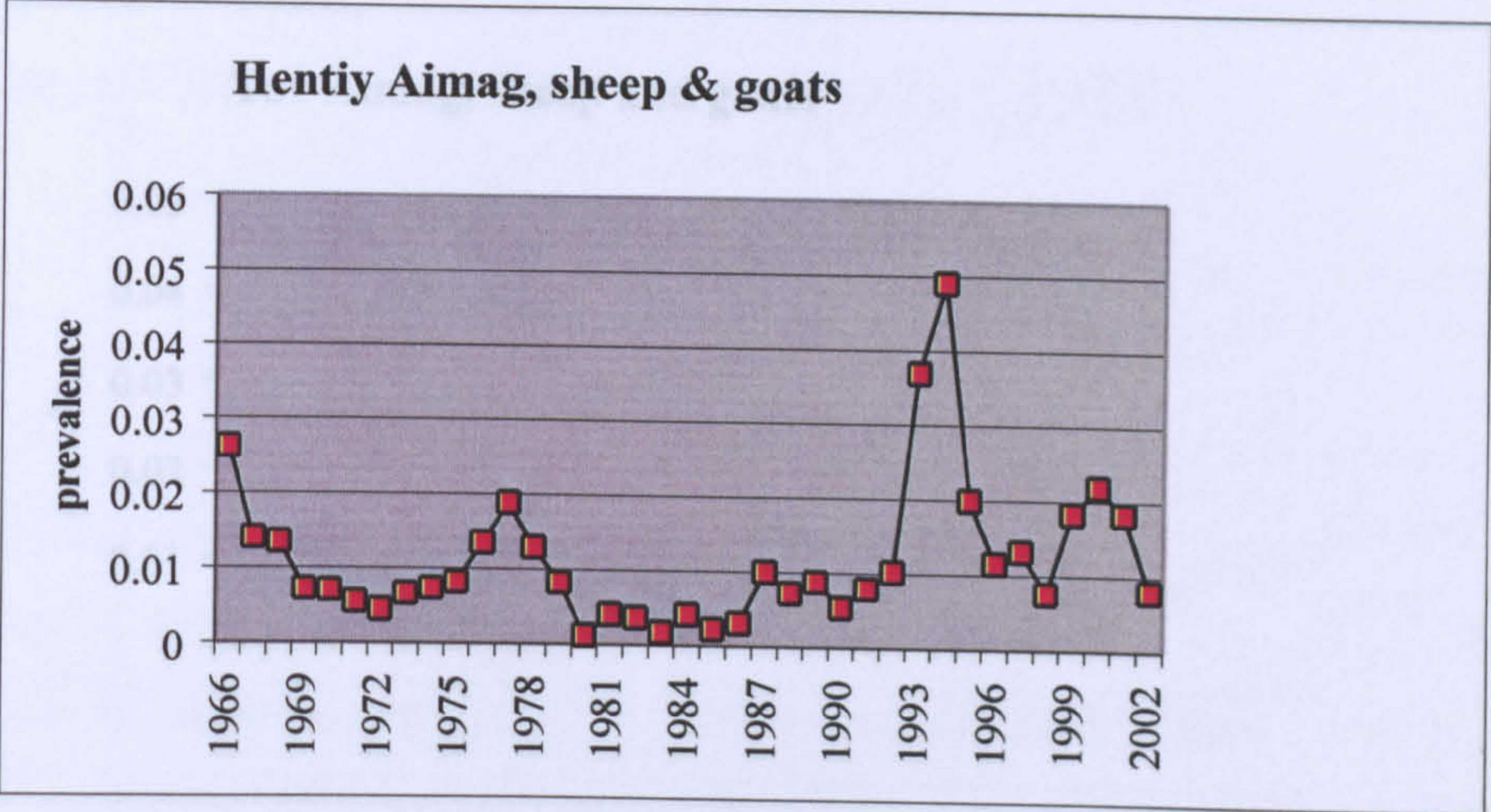




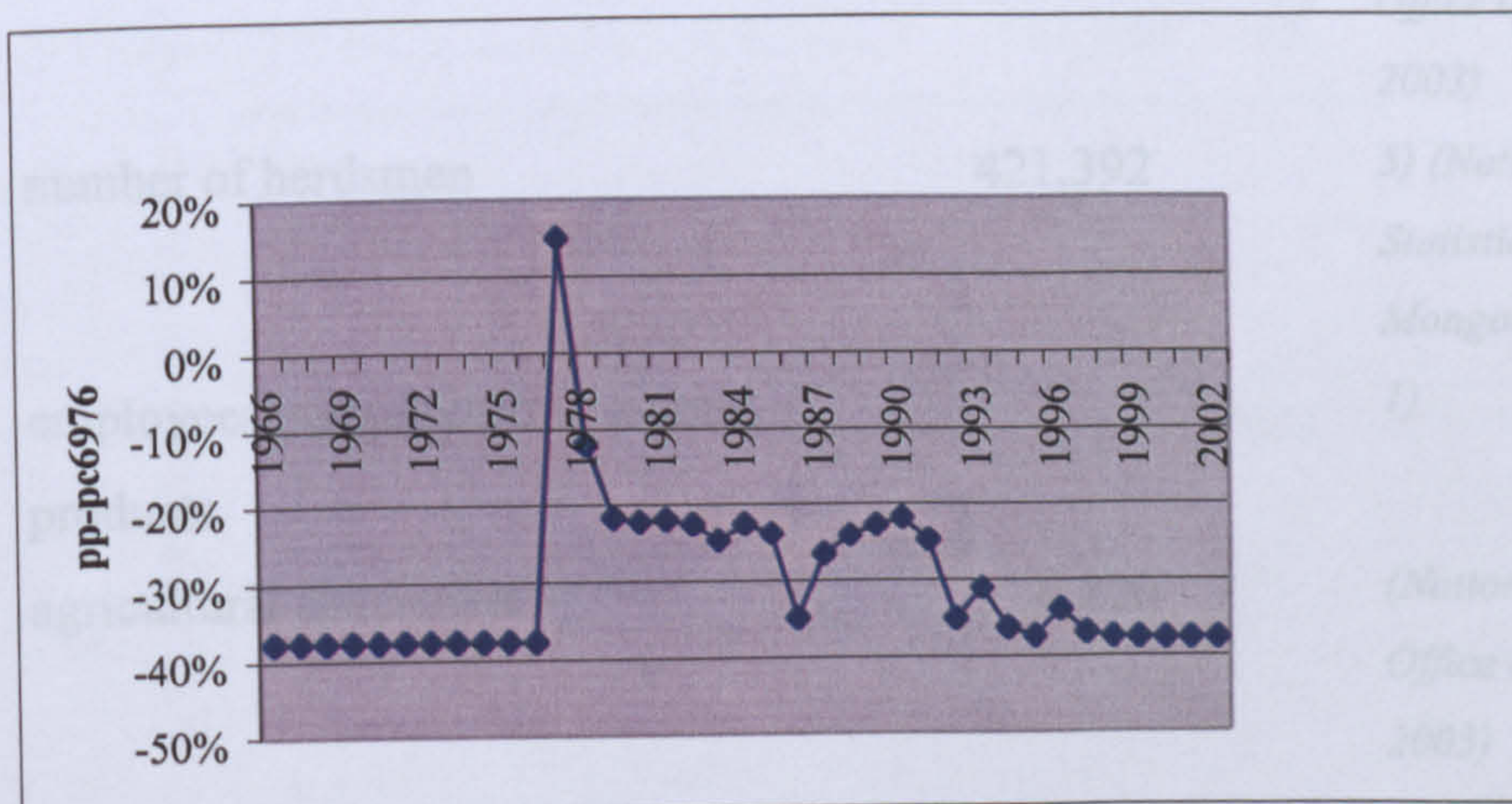
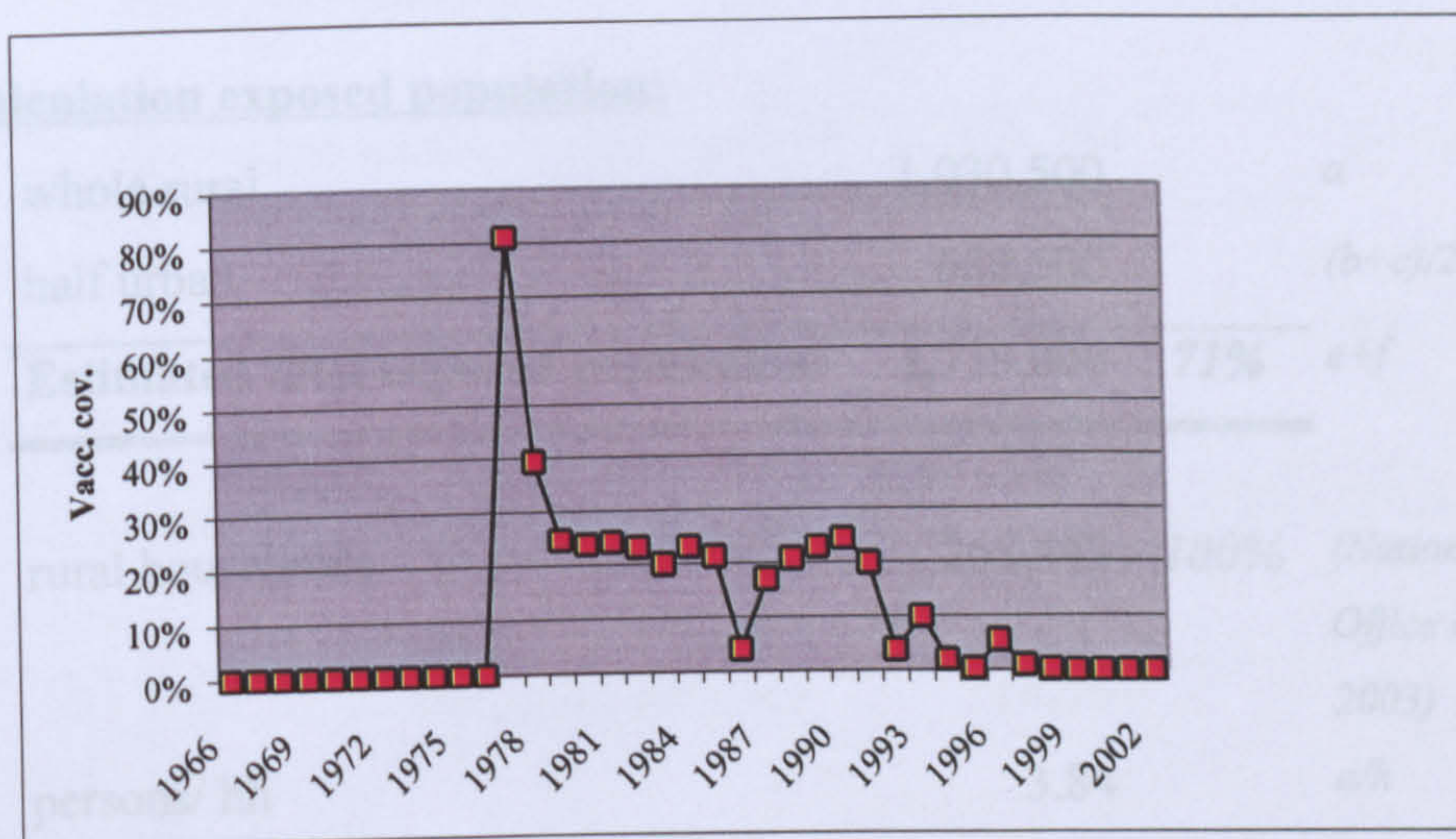
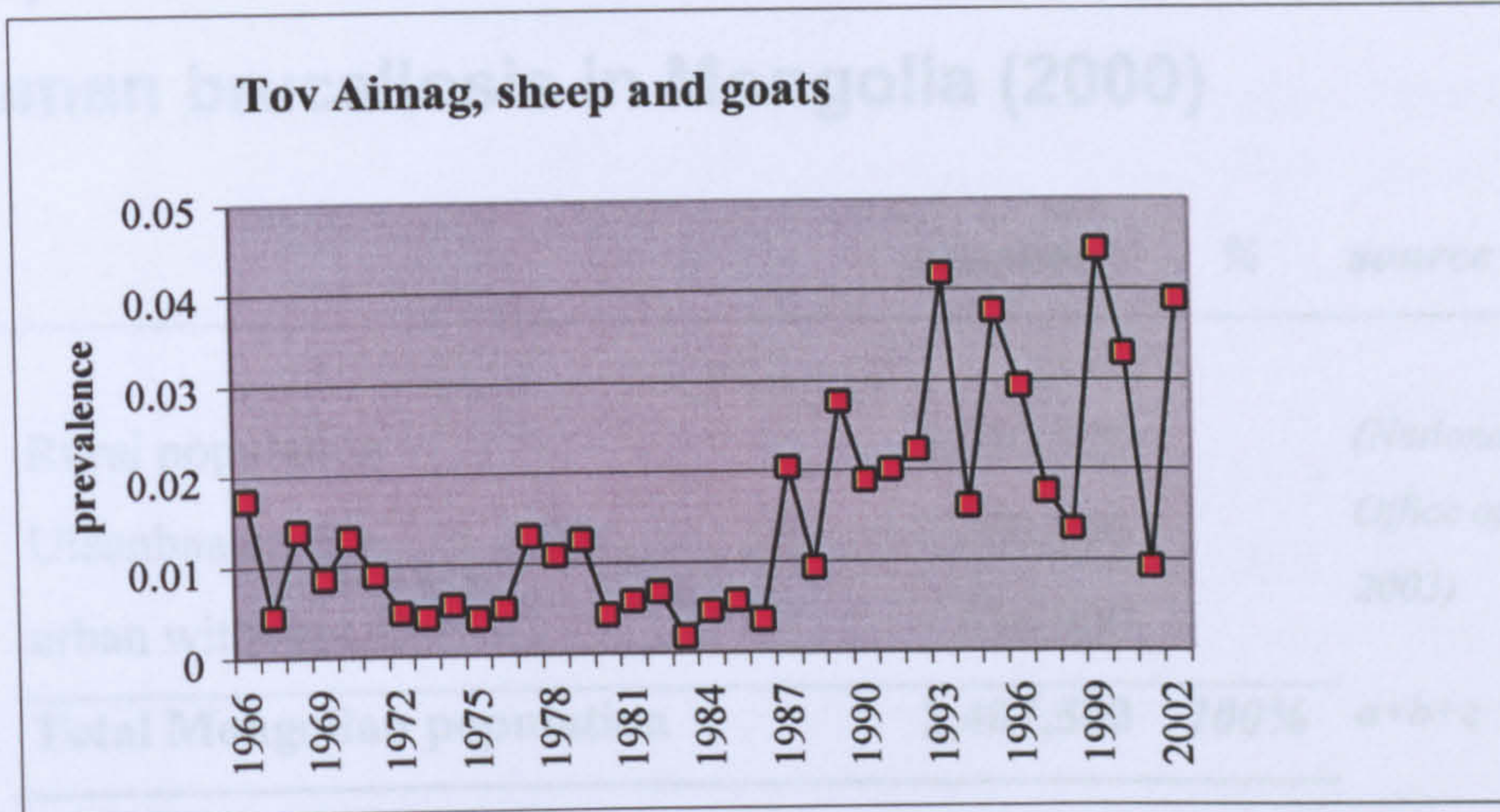
Dornod Aimag, sheep & goats







Appendix 7.1.: Estimation of under-reporting in human brucellosis in Mongolia (2000)



Appendix 7.1.: Estimation of under-reporting in human brucellosis in Mongolia (2000)

	number	%	source
<i>a</i> Rural population	1,030,500		(National Statistical
<i>b</i> Ulaanbaatar	760,100		Office of Mongolia,
<i>c</i> urban without UB	616,900		2003)
<i>d</i> Total Mongolian population	2,407,500	100%	<i>a+b+c</i>

Calculation exposed population:

<i>e</i> whole rural	1,030,500		<i>a</i>
<i>f</i> half urban	688,500		<i>(b+c)/2</i>
<i>g</i> Estimated total exposed population:	1,719,000	71%	<i>e+f</i>
<i>h</i> rural households	268,443	100%	(National Statistical Office of Mongolia, 2003)
<i>i</i> persons/ hh	3.84		<i>a/h</i>
<i>j</i> herder household	191,526	71%	(National Statistical Office of Mongolia, 2003)
<i>k</i> number of herdsmen	421,392		5) (National Statistical Office of Mongolia, 2003)
<i>l</i> employees manufacturing animal products	?		1)
<i>m</i> agricultural specialists	6,200		(National Statistical Office of Mongolia, 2003)

Calculation infected population:

<i>n</i>	seropositive herders		16%	(State Veterinary & Animal Breeding Department of the Ministry for Food & Agriculture et al, 2001)
<i>o</i>	seropositive herders		25%	(Garin-Bastuji B., 1999)
<i>p</i>	estim. nomadic pop. & agric. specialists	741,431		(<i>i*j</i>)+ <i>m</i>
<i>q</i>	estimated nomadic pop. / total pop		31%	<i>p/d</i>
<i>r</i>	nomadic pop / total pop		26%	5) (Ebright J R et al, 2003)
<i>s</i>	a) Estimation total infected herders:	152,364		$((n+o)/2)*p$
<i>t</i>	exposed pop. minus (herders & agric. spec.)	977,569		<i>g-p</i>
<i>u</i>	estimation seropos. exposed non agric. pop		1.5%	2) (Jezek Z., 1970)
<i>v</i>	b) Estim. total infec. pop. without herders	14,664		<i>t*u</i>
<i>w</i>	Estimated total infected population	167,028	7%	<i>s+v</i>

Calculation population with active

brucellosis:

<i>x</i>	herders with active brucel.		10%	(Garin-Bastuji B., 1999)
<i>y</i>	herders with active brucel.		9%	(State Veterinary & Animal Breeding Department of the Ministry for Food & Agriculture et al, 2001)

<i>z</i>	a) Estimation herders with disease outbreak:	70,807		$((x+y)/2 * p$
<i>aa</i>	No-herder pop with active brucellosis		0.75%	$u/2$
<i>ab</i>	b) Estim. No-herder pop. with active bruc.	7,332		$t * aa$
<i>ac</i>	Estim. total pop with active brucellosis	78,138	3%	$z + ab$

Calculation of reporting

<i>ad</i>	reported cases (=incidence in year 2000)	992		6)
<i>ae</i>	Duration of illness in statistics in years	3		after 3 y.=new case (Roth F. et al, 2003)
<i>af</i>	Estimated number of total reported cases	1,984	0.08%	$ad * 2$ see 3)

Calculation labortory confirmation

<i>ah</i>	estimated laboratory confirmation	3,968	0.16%	$af * 2$ see 4)
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<i>ag</i>	reported cases of active brucellosis	2.54%	af/ac
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- 1) no data, not considered, thus conservative estimation
- 2) Surveys resulted 3% seropositive among non-agricultural pop. (1970s): here half of this rate is taken
- 3) Average duration of illness is estimated at 2 years, as many chronic cases occured
- 4) $af * 2$ (estimation: half of the laboratory confirmed are reported)
- 5) Information used for plausibility check
- 6) (Health Development Centre, Mongolia, 2002) (National Center for Health Development, 2001) (The Directorate of Medical Services, 2002)



A model of animal–human brucellosis transmission in Mongolia

J. Zinsstag^{a,*}, F. Roth^a, D. Orkhon^b, G. Chimed-Ochir^c,
M. Nansalmaa^d, J. Kolar^e, P. Vounatsou^a

^a Swiss Tropical Institute, P.O. Box, CH-4002, Basle, Switzerland

^b Ministry of Public Health, Olympic Street 2, Ulaan Baatar 11, Mongolia

^c Infectious Disease Research Centre, P.O. Box 48, Ulaan Baatar, Mongolia

^d Mongolian Academy of Sciences, Post Office 20A, P.O. Box 8, Ulaan Baatar 210620, Mongolia

^e Podbelohorska 38, CR-150 00 Praha, Czech Republic

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Abstract

We developed a dynamic model of livestock-to-human brucellosis transmission in Mongolia. The compartmental model considers transmission within sheep and cattle populations and the transmission to humans as additive components. The model was fitted to demographic and seroprevalence data (Rose Bengal test) from livestock and annually reported new human brucellosis cases in Mongolia for 1991–1999 prior to the onset of a mass livestock-vaccination campaign (S19 *Brucella abortus* for cattle and Rev1 *Brucella melitensis* for sheep and goat). The vaccination effect was fitted to livestock- and human-brucellosis data from the first 3 years of the vaccination campaign (2000–2002). Parameters were optimized on the basis of the goodness-of-fit (assessed by the deviance). The simultaneously fitted sheep–human and cattle–human contact rates show that 90% of human brucellosis was small-ruminant derived. Average effective reproductive ratios for the year 1999 were 1.2 for sheep and 1.7 for cattle.

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Keywords: *Brucella* spp.; Animal–human transmission model; Livestock vaccination; Sheep; Cattle; Public health; Mongolia

* Corresponding author. Tel.: +41 61 284 81 39; fax: +41 61 284 81 05.

E-mail address: jakob.zinsstag@unibas.ch (J. Zinsstag).

1. Introduction

Brucellosis is one of the world's major zoonoses (Boschioli et al., 2001). Human brucellosis commonly is caused by exposure to infected livestock and livestock products (mostly raw milk and milk products). The clinically most-important causative bacteria in humans are in decreasing order of severity of illness: *Brucella melitensis* (small ruminants), *Brucella abortus* (cattle), *Brucella suis* (pigs) and *Brucella canis* (dogs). There is no recorded transmission of the infection between humans (Krauss et al., 1996) but humans can very rarely infect animals (Parnas et al., 1966). In humans, mortality is negligible, but the illness can last for several years (Madkour, 2001). In animals, brucellosis mainly affects reproduction and fertility, reduces survival of newborns (Sewell and Brocklesby, 1990) and reduces milk yield. Mortality of adult animals is insignificant (Sewell and Brocklesby, 1990).

Control strategies available to prevent human infection are pasteurisation of milk, livestock vaccination and the elimination of infected animals. In Mongolia, after numerous surveys in the 1960s, the World Health Organization (WHO) came to the conclusion that livestock vaccination was the only effective way to control brucellosis. The production of livestock vaccines successfully was established in the early 1970s and a country-wide mass-vaccination program of livestock planned for 11 years started in 1975 under difficult field conditions. The vaccination of livestock successfully reduced human incidence of brucellosis to less than one case per 10,000 per year (Kolar, 1977). The vaccination program was interrupted in the early 1980s due to the end of WHO assistance and democratic reform followed by the shift away from dependence on the former Soviet Union in 1990; human brucellosis re-emerged. Based on a request of the Mongolian Government to WHO to provide assistance again in brucellosis control and to resurrect the vaccination program and recommendations made to the WHO and the Mongolian government (Garin-Bastuji, 1999), a whole-herd vaccination strategy covering 10 years was developed (Mikolon, 1999) to start in 2000.

Available models of brucellosis transmission consider only transmission between single livestock species and no transmission to humans, although brucellosis is transmitted to humans from both small ruminants (sheep and goat) and cattle (Roe, 1977; Carpenter et al., 1987; Dalrymple, 1993; Gonzalez-Guzman and Naulin, 1994). Our main objective was to develop a dynamic model of livestock-to-human brucellosis transmission to estimate demographic (birth rate, mortality) and transmission parameters (contact rates) between livestock and livestock to humans as an underlying basis for a cost-effectiveness analysis of a nation-wide mass-vaccination programme for livestock, which is reported elsewhere (Roth et al., 2003). Minor objectives were: (1) to fit vaccination parameters to data on the first 3 years of the national brucellosis livestock-vaccination campaign in Mongolia and (2) to simulate the brucellosis epidemic with and without specified interventions.

2. Materials and methods

2.1. Data collection

Livestock demographic data were provided by the Mongolian Statistical Office (Mongolian Statistical Yearbook, 1999). Animal brucellosis-seroprevalence survey data

(Rose Bengal; RBT) were provided at the provincial level for cattle and sheep for the years 1990–1999 by the Ministry of Agriculture for the model fit without intervention (Appendix A). The RBT is a simple and inexpensive test to detect antibodies against *Brucella* spp. in serum of many species. For the diagnosis of *B. melitensis* in sheep its sensitivity and specificity were recently estimated at 95 and 100% against culture (Ferreira et al., 2003). However, other authors point out that sensitivity and specificity vary in different settings and depending on investigators (Maichomo et al., 1998; Ostanello et al., 1999; MacMillan, 1997). The seroprevalence in cattle and sheep varied between 0.5 and 3%. (S.E. $\leq 0.045\%$ in cattle and $\leq 0.035\%$ in sheep). Data on the ongoing mass-vaccination campaign were provided from 2000 to 2002 (Appendix A). The quality of the available official national demographic and seroprevalence data presented could not be checked, but ongoing studies on brucellosis in livestock indicate that the reported seroprevalence is underestimated (A. Mikolon, personal communication). Our analysis is thus rather conservative with regard to the importance of brucellosis and was restricted to seroprevalences provided by the RBT. Baseline disease data on reported cumulative incidence of human brucellosis listed by province (Mongolian: Aimag), for 1990–1999, were provided by the Infectious Disease Research Institute (IDRI) in Ulaan Baatar. The human-brucellosis data are comprised of annually reported human cases that were diagnosed clinically and in general confirmed by two of the following tests (RBT, Huddelson or Wright). These tests were not standardized between the different Mongolian provinces. However, Mongolian physicians have long-standing experience with diagnosing clinical brucellosis and we see no reason to suspect that accuracy of clinical diagnosis would have changed in the decade of data we used. *Brucella* cultivation from human patients rarely is attempted.

2.2. Model

2.2.1. General considerations

We developed a deterministic model with stochastic parameter specification of animal-to-human brucellosis transmission in steps of 1 year (t) (Table 1 and Fig. 1), which is adapted to the availability of data for validation. Because only data on seropositive animals were available, we used (instead of “infectious” and “recovered” compartments), only one “seropositive” compartment. We considered transmission between sheep, between cattle, and from both livestock species to humans. We omitted the transmission between goats and from goats to humans due to the lack of data. We neither account for brucellosis in yaks and camels, nor for transmission between cattle and small ruminants for the same reason. Sheep total-population data are only available for the years 1995–1999. We reconstructed the total population for the years 1990–1994 by linear regression on the years 1995–1999 in analogy to the almost-linear growth of the cattle population. A posteriori, the sheep-brucellosis component was refitted to data on sheep population and brucellosis prevalence found after extensive archive studies in Ulaan Baatar for the years 1984–1999 (F. Roth, personal communication). Brucellosis affects mostly fertility and milk production. In the model, we consider a seroprevalence-dependent effect on sheep and cattle birth rates (Bernues et al., 1997) (see Section 2.3, Fig. 1, Table 1, Appendix B), e.g.

Table 1

List of fitted parameters to brucellosis transmission between sheep, cattle and humans and from sheep to human and cattle to humans with their 95% confidence limits and units (Figs. 2 and 3)

Parameter (symbol and description)	Estimate	95% confidence limits	Unit (remarks)	Distributions used in the sensitivity analyses
Sheep				
α_s Sheep birth rate	0.811	n.e., 0.83	Year ⁻¹	Triangular (0.81, 0.826, 0.818)
β_s Sheep contact rate	1.56 e ⁻⁷	n.e., 1.60 e ⁻⁷	(Sheep * year) ⁻¹	Triangular (1.69 e ⁻⁷ , 1.5743 e ⁻⁷ , 1.53422 e ⁻⁷)
β_{sh} Sheep-to-human contact rate	1.127 e ⁻⁸	1.124 e ⁻⁸ , 1.127 e ⁻⁸	(Sheep * year) ⁻¹	Triangular (1.12 e ⁻⁸ , 1.1279 e ⁻⁸ , 1.12738 e ⁻⁸)
γ_s Proportion of infectious seropositive sheep	Uniform (0.2, 0.8)	–	Straight proportion	–
ε_s Immunity-loss parameter of seropositive sheep	0	–	Year ⁻¹	Uniform (0, 0.022)
μ_s Mortality rate of sheep	0.78	0.774, 0.786	Year ⁻¹	Triangular (0.81, 0.826, 0.818)
δ_s Snow-storm extra mortality in sheep	0.106	–	Year ⁻¹	–
Cattle				
α_c Cattle birth rate	0.273	n.e., n.e.	Year ⁻¹	Uniform (0.256, 0.285)
β_c Cattle contact rate	3.49 e ⁻⁷	n.e., n.e.	(Cattle * year) ⁻¹	Triangular (3 e ⁻⁷ , 3.49 e ⁻⁷ , 4 e ⁻⁷)
β_{ch} Cattle-to-human contact rate	2.11 e ⁻⁹	2.09 e ⁻⁹ , 2.13 e ⁻⁹	(Cattle * year) ⁻¹	Triangular (2.09 e ⁻⁷ , 2.14 e ⁻⁷ , 2.11 e ⁻⁷)
γ_c Proportion of infectious seropositive cattle	Uniform (0.1, 0.85)	–	Straight proportion	–
ε_c Cattle immunity-loss constant	0	–	Year ⁻¹	–
μ_c Cattle mortality rate	0.226	n.e., n.e.	Year ⁻¹	Uniform (0.256, 0.285)
δ_c Snow-storm extra mortality in cattle	0.221	–	Year ⁻¹	–
Humans				
α_h Human birth rate	0.018	0.012, 0.023	Year ⁻¹	Triangular (0.012, 0.023, 0.0181)
μ_h Human mortality rate	0.003	0.0001, 0.02	Year ⁻¹	Triangular (0.0001, 0.02, 0.0031)
Parameter (symbol and description)				
			Assumption	Unit
λ End of registry constant			0.5 (definition)	Year ⁻¹
κ Registry			1	Year ⁻¹
η Prevalence dependent decrease of birth rate in sheep and cattle			Uniform (0.15, 0.5)	Straight proportion
t Time			Steps of 1	Year

Distributions listed were used in the sensitivity analyses without interventions (Figs. 2–4) and with brucellosis mass vaccination (Fig. 5). n.e.: not estimated by the fitting algorithm; *: multiplication.

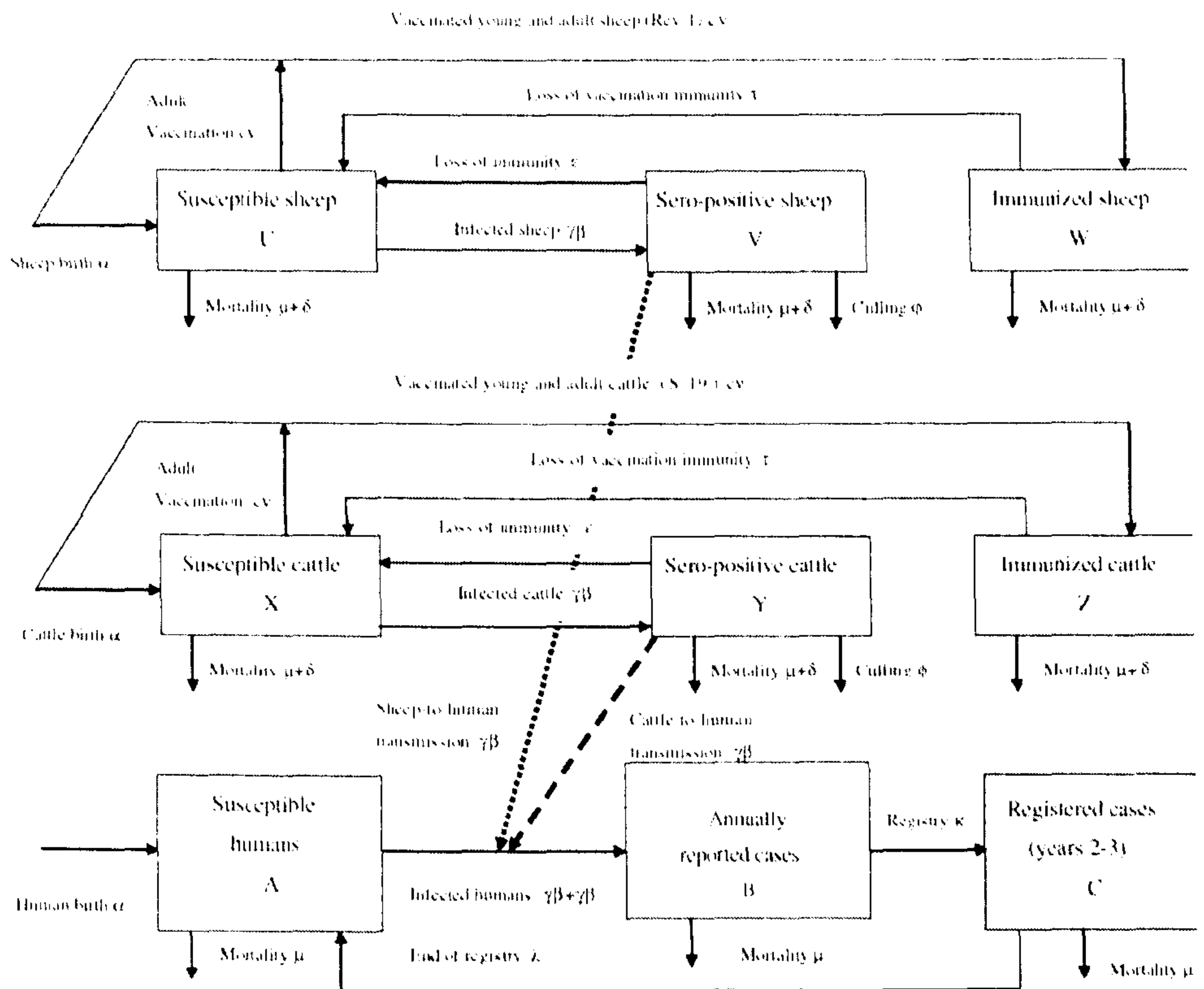


Fig. 1. Model for joint human–animal brucellosis transmission in Mongolia modified after Roth et al. (2003), with permission from the Bulletin of the World Health Organization.

for cattle

$$\alpha_{c(\text{effective})} = \alpha_{c(\text{baseline})} \left(1 - \left(\eta \left(\frac{Y}{(X + Y + Z)} \right) \right) \right) \quad (1)$$

where η is the prevalence-dependent reduction of birth rates α_c (including abortions) among the seropositive (expressed as uniform probability distribution, Table 1), X the number of susceptible, Y the number of seropositive and Z is the number of vaccine-protected cattle. The incidence (Fig. 1, infected sheep and cattle) is calculated by the product of γ_c (γ_s) (proportion of infectious), expressed as uniform probability distribution (see Table 1), the β (contact rate), the number of susceptible X (or U) and the number of seropositive Y (or V). Thus, the incidence in cattle is

$$\text{incidence}_{\text{cattle}} = \gamma_c \beta_c X Y \quad (2)$$

2.3. Compartments and flows between compartments

Compartment U (Fig. 1) is the susceptible-sheep population (national sheep population of Mongolia minus V). Compartment V is the brucellosis-seropositive population. The size of V is obtained by multiplying the national sheep population with the prevalence estimated in annual surveys. Compartment W is the brucellosis-vaccinated sheep (Rev1). Compartment X is the susceptible-cattle population (national cattle population of Mongolia minus Y). Compartment Y is the brucellosis-seropositive cattle population. Its size is obtained by multiplying the national cattle population with the prevalence estimated in annual surveys. Compartment Z is the brucellosis-vaccinated cattle (S19 vaccine).

Compartment A represents the whole Mongolian human population, because precise estimates of the population at risk are not available. In Mongolia, reported Brucellosis patients are officially registered for 3 years. Compartment B represents the annually newly registered brucellosis patients and compartment C the registered patients between years 2 and 3 of state registration, after which they are considered no longer as registered brucellosis patients. Thus, the annual rate of flow (κ) from B to C (Fig. 1, registry) by definition = 1 and the end-of-registry constant = 0.5, i.e. inverse of the duration of registration in compartment (C). In this way, the model takes Mongolian health policy into account.

The descriptions of flows (Fig. 1) are as follows: flows into the susceptible-sheep compartment (U) are *sheep birth*, *loss of immunity* and *loss of vaccination immunity*: *sheep birth* (unit: sheep/year) = $\alpha_s(U + V + W)(1 - (\eta(V/(U + V + W))))(1 - c_{ys}\nu_{Rev1})$, where α_s is the birth rate of sheep (Table 1), multiplied by the sum of all compartments ($U + V + W$). This term is again multiplied by a seroprevalence—($U/(U + V + W)$) dependent decrease of sheep birth rate ($1 - \eta$) (Bernues et al., 1997). For the simulation of intervention, the whole term is multiplied by 1 minus the proportion of vaccination protected sheep ($c_{ys}\nu_{Rev1}$) (Table 2), where c_{ys} is the vaccination coverage of newborn sheep and ν_{Rev1} is the proportion of reduction of transmission of Rev1 vaccine (see below). The *loss of immunity of sheep* (unit: sheep/year) is considered by the term $\varepsilon_s V$, where ε_s is an immunity-loss parameter (Table 1) multiplied with compartment V (seropositive sheep). *Loss of vaccination immunity in sheep (Rev1)* (unit: sheep/year) = $\tau_{Rev1} W$, where τ_{Rev1} is a vaccination-immunity-loss parameter multiplied with compartment W (immunized sheep). Flows out of compartment U are *mortality of susceptible sheep*, *infected sheep* and *vaccinated young and adult sheep (Rev1)*: *mortality* (unit: sheep/year) of susceptible sheep = $-(\mu_s U + \delta_s U)$, where μ_s is the mortality rate of sheep and δ_s is the extra mortality rate of sheep due to the snow-storm disasters (see below). *Infected sheep* (=incidence in sheep) (unit: sheep/year) is = $-\gamma_s \beta_s UV$ in analogy to Eq. (2) (see above). *Vaccinated young and adult sheep (Rev1)* (unit: sheep/year) is composed of the proportion of protected young sheep as fraction $-c_{ys}\nu_{Rev1}$ of *sheep birth*, and adult sheep vaccination = $-c_{as}\nu_{Rev1} U/3$, where c_{as} is the coverage of adult-sheep vaccination and ν_{Rev1} is the efficacy of Rev1 vaccine. The division by three of the adult vaccination accounts for two rounds of adult vaccination in 6 years. Flows into compartment U appear as positive terms and flows out of compartment U as negative terms in the differential Eq. (A.1) dU/dt in Appendix B. All other differential equations are constructed in the same way.

Flows going into the compartment of seropositive sheep V are *infected sheep* as described above. Flows out of compartment V are *mortality of seropositive sheep* *loss of*

Table 2
Intervention-related parameters used in the model

Parameter (symbol and description)	Assumption	Unit (remarks)
Sheep		
ν_{Rev1} Vaccine efficacy of Rev1	0.65	Straight proportion
τ_{Rev1} Inverse duration of vaccination protection of Rev1	Uniform (0.2, 0.25)	Year ⁻¹
c_{as} Vaccination coverage adult sheep	Scenario no vaccination = 0 Scenario 5065 = 0.5 Scenario 8065 = 0.8 Scenario 80100 = 0.8	Year ⁻¹
c_{ys} Vaccination coverage young sheep	Scenario no vaccination = 0 Scenario 5065 = 0.5 Scenario 8065 = 0.8 Scenario 80100 = 0.8	Year ⁻¹
φ_s Proportion tested and slaughtered sheep	Scenarios with and without vaccination = 0 Scenario test and slaughter 40% = 0.4	Year ⁻¹
Cattle		
ν_{S19} Vaccine efficacy of S19	0.65	Straight proportion
τ_{S19} Inverse duration of vaccination protection of S19	Uniform (0.125, 0.142)	Year ⁻¹
c_{ac} Vaccination coverage adult cattle	Scenario no vaccination = 0 Scenario 5065 = 0.5 Scenario 8065 = 0.8 Scenario 80100 = 0.8	Year ⁻¹
c_{yc} Vaccination coverage young cattle	Scenario no vaccination = 0 Scenario 5065 = 0.5 Scenario 8065 = 0.8 Scenario 80100 = 0.8	Year ⁻¹
φ_c Proportion tested and slaughtered cattle	Scenarios with and without vaccination = 0 Scenario test and slaughter 40% = 0.4	Year ⁻¹

immunity and test and slaughter of seropositive sheep. Mortality of seropositive sheep $V = -(\mu_s V + \delta_s V)$ is analogous to the mortality of susceptible sheep (see above) but for the compartment V . Test and slaughter (unit: sheep/year) of seropositive sheep = $-\varphi_s V$, where φ_s is the proportion of tested and slaughtered sheep multiplied with V . The loss of immunity is already described above but appears as negative term $-\varepsilon_s V$ in the differential equation (A.2) (dV/dt) in Appendix B. Flows going into the compartment of immunized sheep W are vaccinated young and adult sheep (Rev1): adult-sheep vaccination = $(c_{as} \nu_{Rev1} U)/3$ (see above) and young-sheep vaccination = $(c_{ys} \nu_{Rev1})(\alpha_s(U + V + W)(1 - (\eta(V/(U + V + W))))$. The latter term expresses the fraction of newborn sheep being protected from transmission (see above: sheep birth). Flows going out of compartment W are mortality of immunized sheep and loss of vaccination immunity of sheep. Mortality of immunized sheep W is $-(\mu_s W + \delta_s W)$ in analogy to the mortality of susceptible and seropositive sheep but

multiplied with W . The *loss of vaccination immunity* (unit: sheep/year) of sheep = $-\tau_{\text{RevI}}W$ is analogous to the description above but as a negative term. Adult- and young-sheep vaccination appear as positive terms in differential equation (A.3) (dW/dt) in Appendix B, whereas mortality of immunized sheep and the loss of vaccination immunity of sheep are negative terms.

Flows into the cattle compartments are analogous to those for sheep. Vaccinations of newborn cattle are accounted by multiplying the whole term with $(1 - (c_{yc}v_{S19}))$ where c_{yc} (Table 2) is the vaccination coverage of young cattle and v_{S19} is the proportion of reduction of transmission resulting from the S19 vaccine (see below).

Flows into compartment A (susceptible humans) are *human birth* and *end of registry*. *Human birth* (unit: humans/year) = $\alpha_h(A + B + C)$ where α_h is the human birth rate multiplied by the sum of all human compartments. *End of registry* (unit: humans/year) = λC , where λ is the end-of-registry (i.e. end of any one person's inclusion in the registry) constant multiplied with compartment C (registered cases in years 2–3). Flows out of A are *infected humans* and *mortality* of susceptible humans. *Infected humans* (unit: humans/year) (animal-to-human transmission) = $-((\gamma_c\beta_{ch}AY) + (\gamma_s\beta_{sh}AV))$ is described below. *Mortality* (unit: humans/year) of susceptible humans is = $\mu_h A$, where μ_h is the mortality rate of humans multiplied with compartment A . (Changes of compartment A are expressed in Eq. (A.7) (dA/dt) in Appendix B.) Flows into compartment B are *infected humans* = $((\gamma_c\beta_{ch}AY) + (\gamma_s\beta_{sh}AV))$, which take a positive sign for this compartment. Flows out of B are *mortality* and *registry*. *Mortality* (unit: humans/year) of annually reported cases = $\mu_h B$ in analogy for compartment A . *Registry* (unit: humans/year) = $-\kappa B$, with the registry constant $\kappa = 1$ as outlined above. Eq. (A.8) (dB/dt) considers changes of annually reported cases. Finally, flows into compartment C are *registry* cases and flows out of C are *end of registry* and *mortality* of registered cases (years 2–3). *Registry* = κB and *end of registry* (unit: humans/year) = $-\lambda C$, where λ is the end of registry parameter multiplied with C . *Mortality* of registered cases = $-\mu_h C$ in the same way as for compartments A and B . (Eq. (A.9), (dC/dt) specifies changes among the registered cases.)

2.4. Fitting the transmission model

The fitting of the model to the data was done with VensimTM systems-analysis software (Ventana Systems Inc., 60 Jacob Gates Road, Harvard, MA, USA; www.vensim.com) using the Powell nonlinear maximum-likelihood optimization algorithm (Press et al., 1991). Parameters were optimized on the basis of the goodness-of-fit, which is called “payoff” in Vensim software. The payoff compares the log likelihood of the current model with the log likelihood of a perfect model (having as many parameters as data points). The best model is the one with smallest payoff. In the first step, mortality and birth rates were optimized for the susceptible sheep (U), cattle (X) and humans (A) (Fig. 1). Birth rates were expressed proportionally to the total populations; mortality parameters in livestock included natural mortality and off take. In the second step, the transmissions within sheep and within cattle were fitted by fixing the demographic parameters. To fit the transmission process, the proportions of infected V and Y were expressed as uniform probability distributions and their boundaries were varied to identify the best fit (in terms of the deviance) of contact rates for the transmission between sheep and between cattle and the

loss of immunity. The transmission to humans is expressed as additive contributions of transmission from sheep and cattle to humans (Fig. 1, sheep-to-human transmission; cattle-to-human transmission):

$$(\gamma_{\text{sheep}}\beta_{\text{sheep}}AV) + (\gamma_{\text{cattle}}\beta_{\text{cattle}}AY) \quad (3)$$

where A is the susceptible human population. The effective reproductive ratio and threshold vaccination coverage were estimated according to Scott and Smith (1994), using the confidence limits of the proportions of infectious animals obtained during the fitting process. Long-term properties were investigated by keeping the animal populations stable from year 1999 onwards (in keeping with the limited carrying capacity of Mongolian pasture).

2.5. Fitting of the vaccination interventions

In the year 2000, the Mongolian authorities started the mass vaccination of their ruminants. However, the onset of the vaccination campaign coincided with consecutive snow-storm disasters in the winters 1999–2002 and the loss of >7 million animals. (A concurrent outbreak of foot-and-mouth disease in 2001 was not taken separately into account because of the lack of disease-specific data.) These massive demographic changes had to be considered for the fitting and validation of the vaccination campaign. Thus, the demographic change of the snow-storm disasters were fitted as an extra mortality from 1999 to 2002. The estimated mortality rates of cattle δ_c and sheep δ_s due to the snow-storm are 22 and 10% per year, respectively. The extra snow-storm mortalities were used for the fitting process of the vaccination campaign but not for the simulations of the different vaccination scenarios (see below). For the fitting of the vaccination campaign, the vaccination efficacy and vaccination coverage (see below) were optimized against the reported seroprevalence of brucellosis in sheep and cattle and the reported cases of human brucellosis.

2.6. Simulation of vaccination and test-and-slaughter scenarios

The current practice in Mongolia (since 1990) consists of low-level surveillance, with occasionally required testing of livestock herds followed by voluntary slaughter of seropositive animals without compensation. The present vaccination strategy (since 2000) aims to vaccinate all adult animals twice within 6 years (1/3 of the total adult population per year). All animals born during the 10 years of the plan will be vaccinated once (at <1 year of age). The reported efficacy in reducing transmission was measured as the prevented fraction $(1 - R)$, where R is the relative risk of disease in those who received the intervention compared to those who do not (Smith and Morrow, 1991). The vaccines used in cattle (Strain B19, *B. abortus*) and small ruminants (Rev1, *B. melitensis*) should reduce transmission by at least 65% (Nicoletti, 1977). These efficacies include also potential losses due to cold-chain deficiency (Mikolon, personal communication). Vaccine-coverage scenarios were set to 50 and 80% (same scenarios for sheep and cattle). The proportion of protection (PP) is computed as the product of the reduction of transmission $\nu_{(\text{Rev1};\text{S19})}$ of the respective vaccine and the vaccination coverage $c_{(\text{ys};\text{as};\text{yc};\text{ac})}$ (Eq. (4)). The proportion of protection of vaccinated young

and adult sheep and young and adult cattle were the product of vaccine-related reduction of transmission and vaccination coverage.

$$PP = cv \quad (4)$$

Three different vaccination scenarios were considered assuming PP of 32% ($v = 65\%$; $c = 50\%$); 52% ($v = 65\%$; $c = 80\%$) and 80% ($v = 100\%$; $c = 80\%$), respectively. For Rev1, we considered an annual loss of vaccination immunity as a random function (uniform (0.2, 0.25); inverses of the duration of vaccination immunity of 4–5 years, WHO, 1998) and for S19, an annual loss of vaccination immunity as a random function (uniform (0.125, 0.142); inverses of duration of vaccination immunity of 7–8 years, AFSSA, 2001). The FAO (J. Otte) suggested including the testing and slaughtering of seropositive animals as a separate intervention. For the simulation, the current capacity of livestock RBT of the Mongolian veterinary laboratories was doubled to consider the proportion φ_c for cattle and φ_s for sheep of 40% of animals being tested and the seropositive animals removed.

2.7. Sensitivity analyses

Sensitivity analyses were done for the fitting of the model without interventions and for the intervention scenarios of 52% PP. For this we used multivariate Monte Carlo sensitivity simulation (MVSS) in VensimTM with 200 simulations over the range of parameters specified in Table 1 (first column on the right). Monte Carlo multivariate sensitivity works by sampling a set of numbers from within bounded domains. To perform one multivariate test, the distribution for each parameter specified is sampled, and the resulting values used in a simulation. All simulations then are summarized by calculating mean values and 95% confidence limits.

3. Results

3.1. Parameter optimization without interventions

The model fitted the susceptible livestock and human populations very well (in Figs. 2a and 3, the observed and fitted values for cattle and humans overlie). The fits to the seropositive sheep and cattle and annually reported human brucellosis cases are presented in Figs. 2b and 3. In Table 1, the fitted parameters with their 95% confidence limits are presented. For sheep and cattle, the unknown proportions infectious were estimated by variation of their boundaries in a uniform distribution. The boundaries with the best payoff were then used in the model. For sheep, best payoff was obtained for a proportion of infectious ranging between 0.2 and 0.8 and for cattle between 0.1 and 0.85. The simultaneously fitted sheep–human and cattle–human contact rates show a contribution of small ruminant-derived human brucellosis of >90% indicating a dominance of *B. melitensis* in human brucellosis. Average effective reproductive ratios for the year 1999 indicated a slow-growing epidemic. The proportion of protection (Eq. (4)) needed to interrupt transmission was 0.46 for sheep and 0.66 for cattle. Long-term properties of the model (assuming stable sheep and cattle populations) predict a peak of seropositive

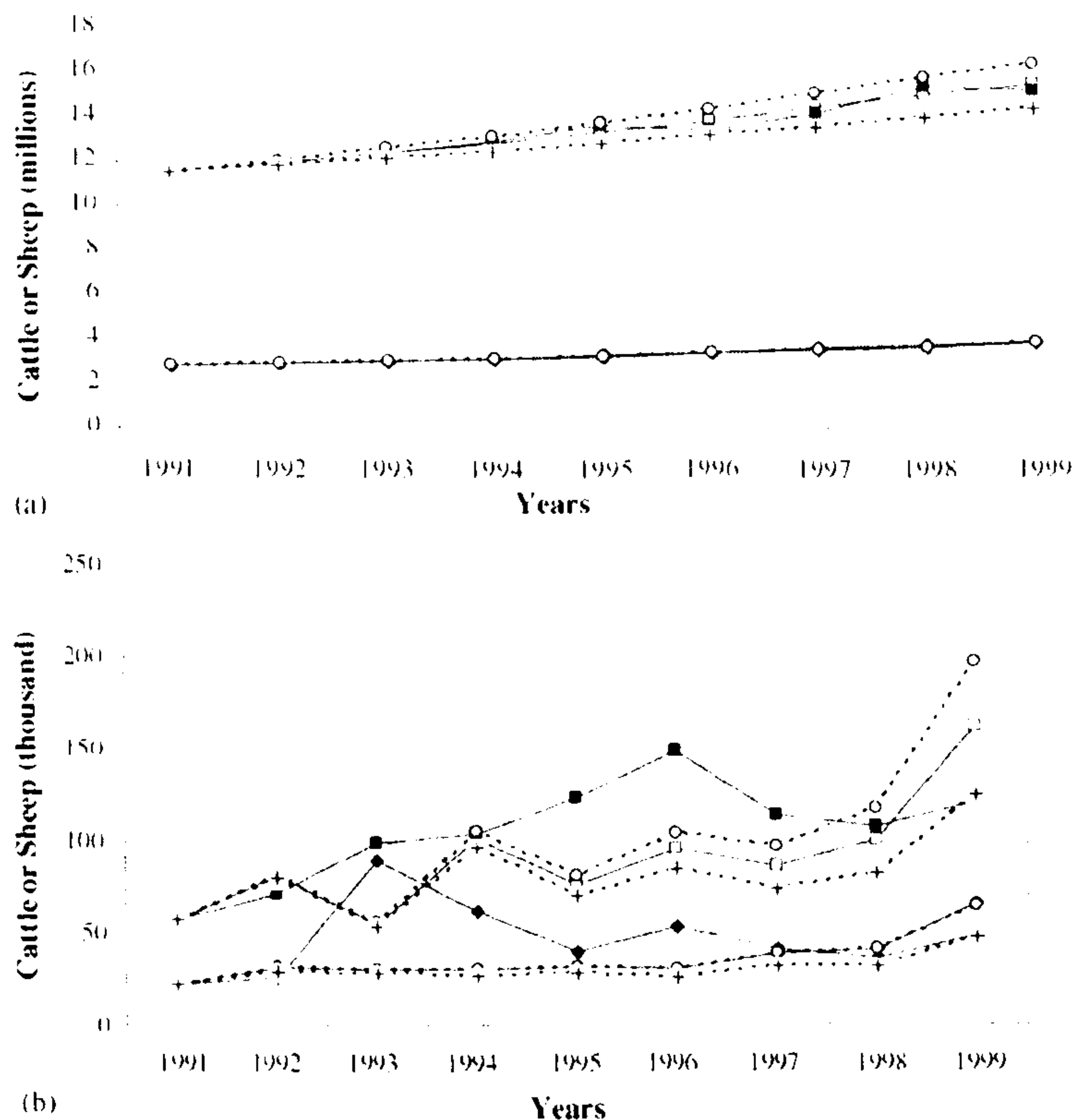


Fig. 2. (a and b) Fit of the model to livestock total population (a) and seropositive (b) data: filled squares, reported sheep population; empty squares, fitted sheep population (95% upper confidence limit, empty circles; and dashed line and 95% lower confidence limit, crosses with dashed line); filled diamonds, reported cattle population; empty diamonds, fitted cattle population (95% upper confidence limit, empty circles; and dashed line and 95% lower confidence limit, crosses with dashed line).

animals between 2020 and 2030 in sheep and between 2030 and 2040 in cattle. In humans, the growth rate between 1991 and 1999 was maintained and human brucellosis would peak, in parallel to that in sheep between 2020 and 2030.

3.2. Fit of vaccination interventions

After fitting the transmission model to the period from 1990 to 1999 (Figs. 2 and 3), during which no vaccination intervention happened, we used the estimated parameters to fit the model to the starting period of the national livestock brucellosis-vaccination campaign from 2000 to 2002. For sheep and cattle, the fitted vaccination campaign follows the trends of the observed seroprevalences. In a simultaneous fit, the fitted coverages are 0.97 (95% CI 0.57, 1) for young sheep (c_{ys}), 1 (not estimated, 1) for adult sheep (c_{as}), 1 (95% CI 0.43, 1) for young cattle (c_{yc}), 1 (0.45, 1) and for adult cattle (c_{ac}) (Table 2). The vaccine efficacies are 0.63 (0.45, 0.84) for Rev1 (v_{Rev1}) and 1 (0.72, 1) for S19 (v_{S19}). The number of

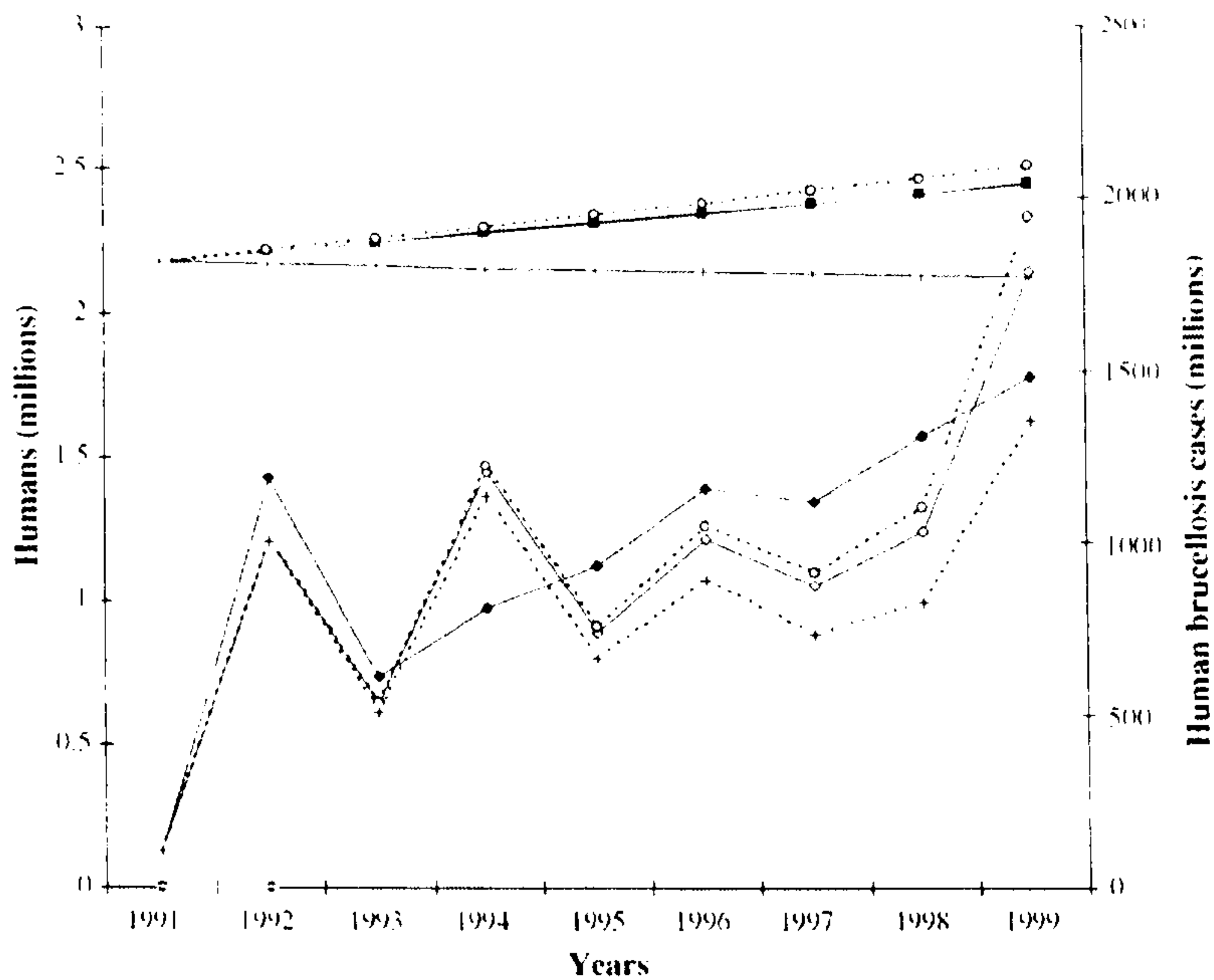


Fig. 3. Fit of the model to human total population and human brucellosis patient data: filled squares, reported susceptible human population; empty squares, fitted susceptible human population (95% upper confidence limit, empty circles; and dashed line and 95% lower confidence limit, crosses with dashed line); filled diamonds, reported human brucellosis cases (compartment *B*); empty diamonds, fitted, human brucellosis cases (95% upper confidence limit; empty circles and dashed line and 95% lower confidence limit, crosses with dashed line).

predicted vaccinated animals overshoots in the first year the reported number and fits better in the consecutive years (data not shown).

3.3. Simulation of specified interventions

3.3.1. Vaccination

A sensitivity analyses with and without the intervention scenario of 52% PP are presented in Figs. 4 and 5. In sheep, the reported seroprevalences for the years 2000–2002 agree best with a trend between the scenarios of 52 and 80% protection (Fig. 6a). In cattle, the simulated vaccination scenarios follow the reported trend for the years 2000–2002 but at a higher level (Fig. 6b).

3.4. Test and slaughter

The simulation of the RBT of 40% of the sheep and the removal of the seropositives predicts a decrease comparable to that in the vaccination scenarios. The test-and-slaughter intervention appeared more effective to reduce brucellosis prevalence in cattle than the vaccination scenarios. However, neither the vaccination nor test-and-slaughter intervention scenarios in cattle lead to elimination by 10 years.

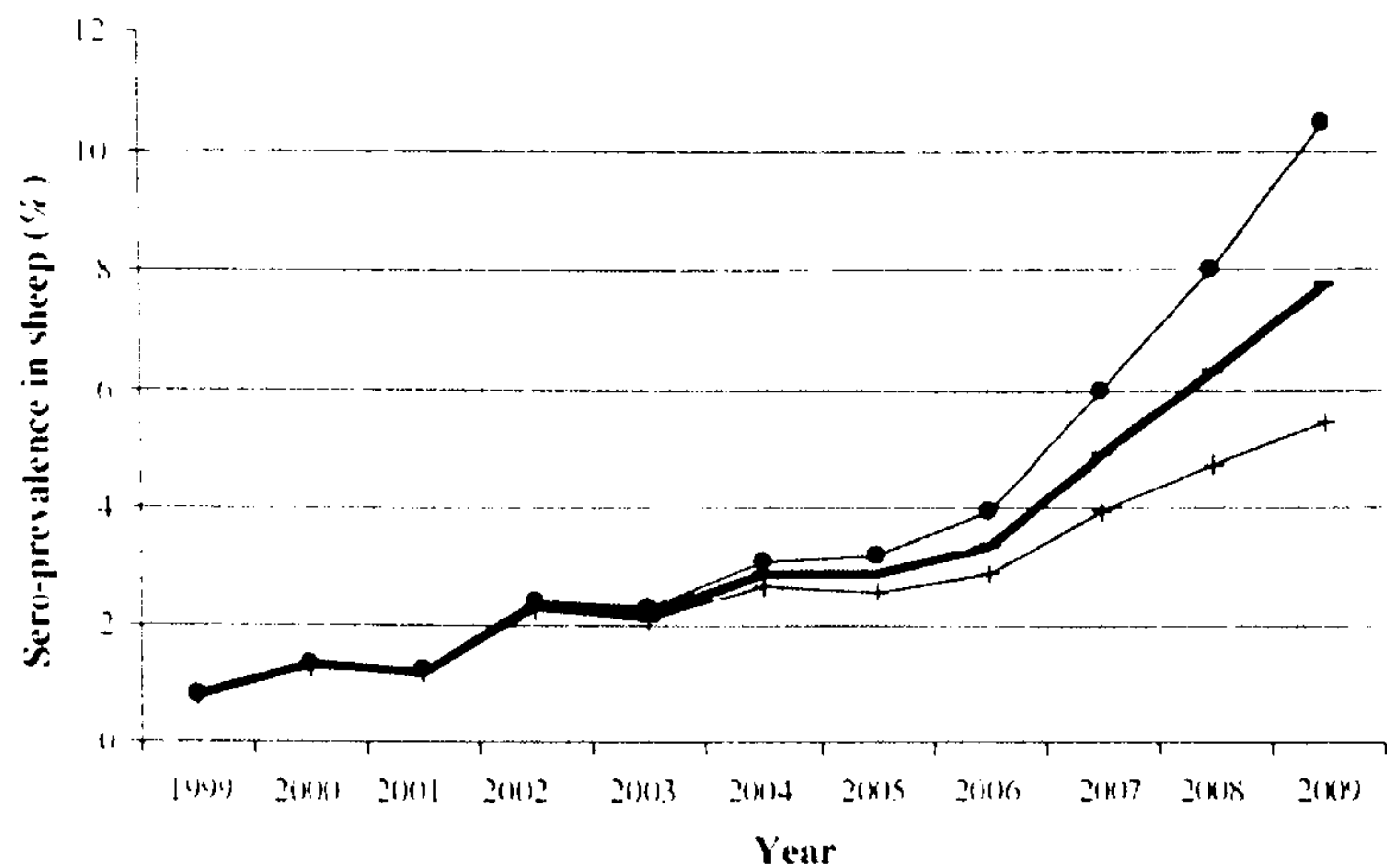


Fig. 4. Sensitivity analysis of the prediction of the brucellosis seroprevalence in sheep without intervention. Bold line: mean; filled circles: upper 95% confidence limit; crosses: lower 95% confidence limit.

4. Discussion

4.1. Model

To our knowledge, this reported model is the first comprehensive dynamic assessment of livestock-to-human brucellosis transmission fitted to a period of transmission with and without intervention. The model conception was adapted to the available data (only

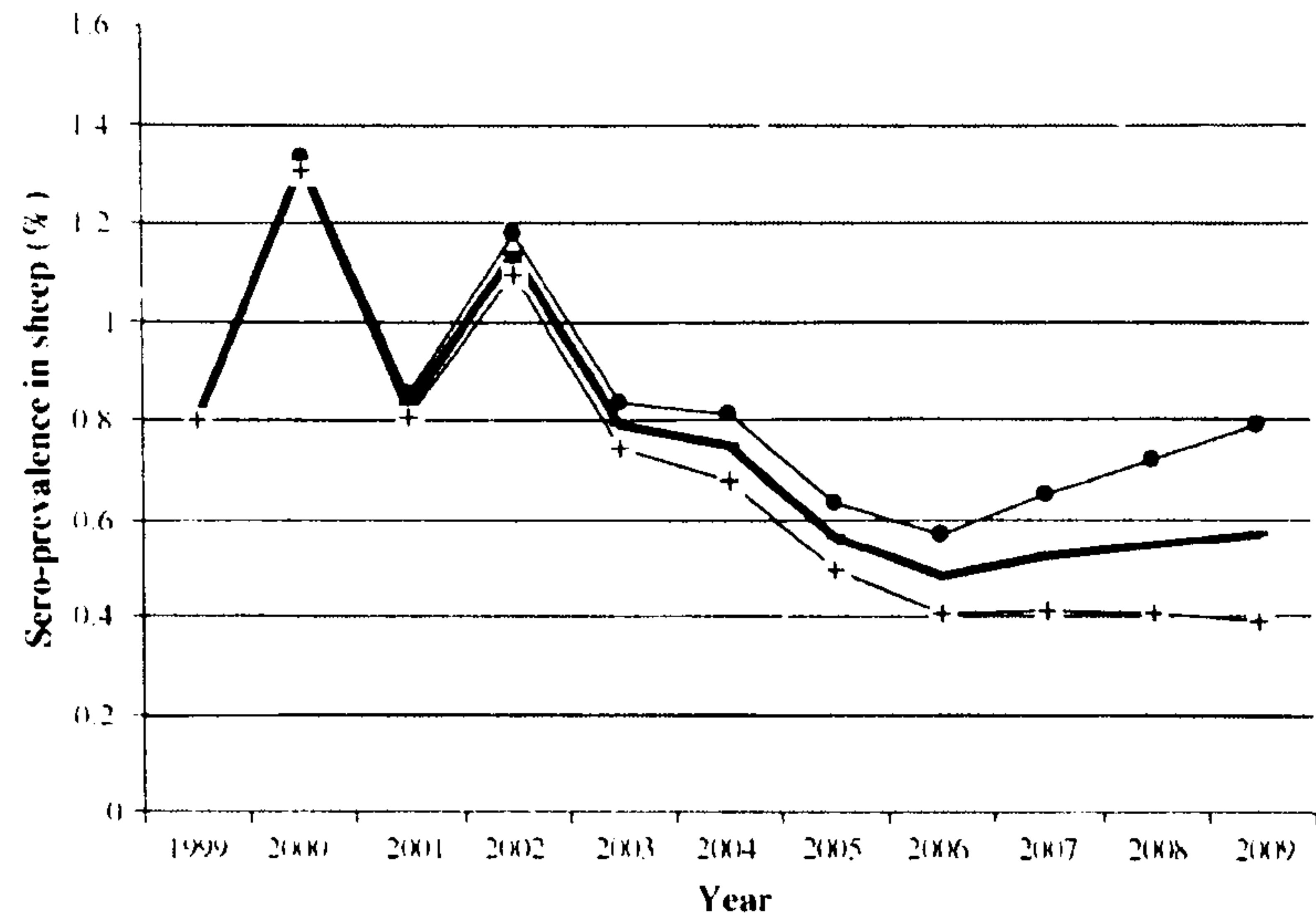


Fig. 5. Sensitivity analysis of the prediction of the brucellosis seroprevalence in sheep with the scenario of 52% PP using Rev1. Bold line: mean; filled circles: upper 95% confidence limit; crosses: lower 95% confidence limit.

seroprevalence data), the needs of economic assessment (Roth et al., 2003) and the consideration of the Mongolian brucellosis patient registry policy to adapt the analysis to the needs and decision pathways of the Mongolian authorities (Habicht et al., 1999). A more general model, without considering Mongolian registration policy, would need to include the duration of untreated human brucellosis and the loss of human post-infection immunity.

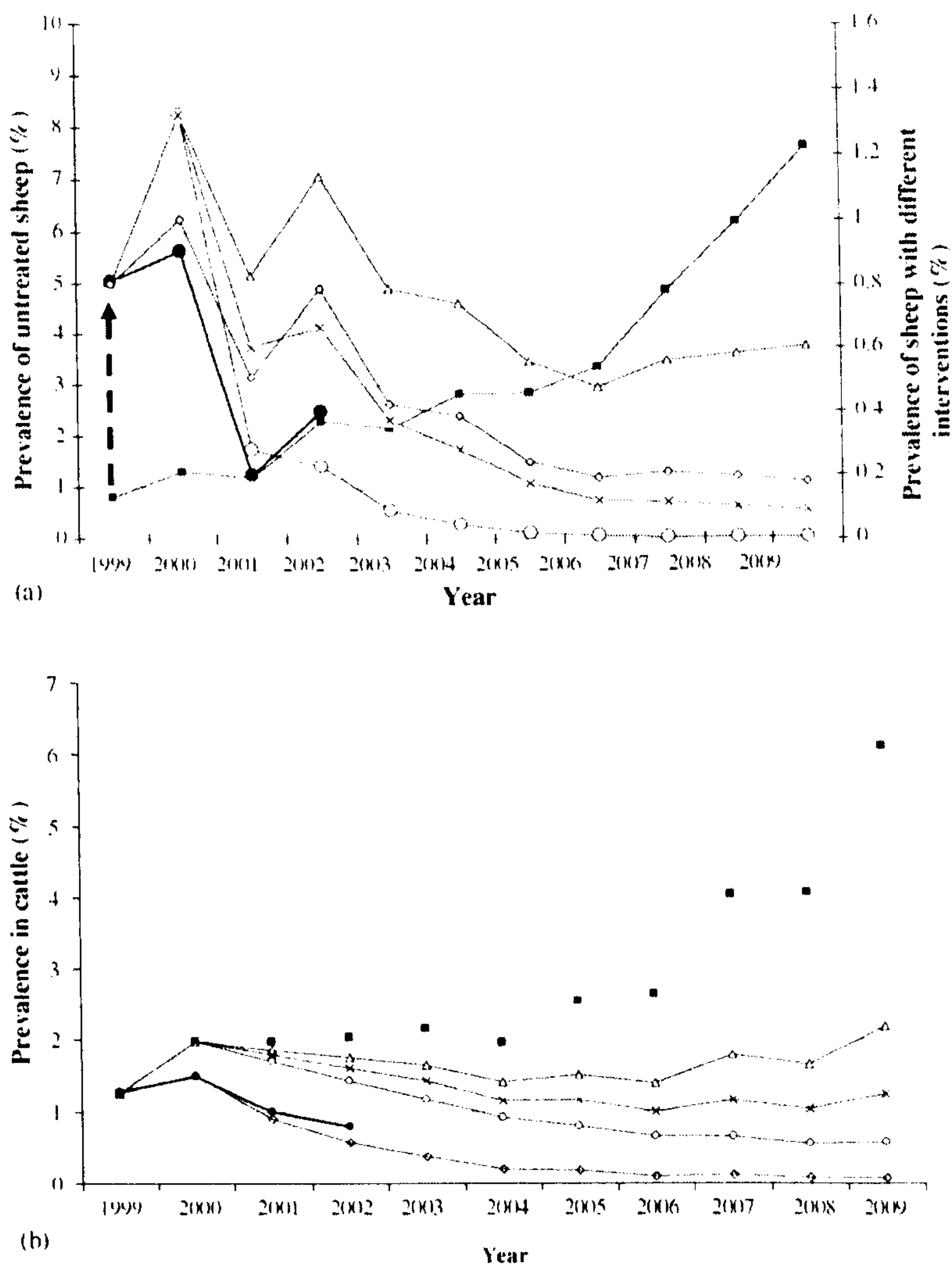


Fig. 6. (a–c) Effect of livestock brucellosis vaccination and test and slaughter of 40% of the sheep and cattle population (a and b) on human annual cumulative brucellosis incidence (c) (filled squares, control scenario; filled circles, reported vaccination; empty triangles, 32% proportion of protection; crosses, 52% proportion of protection; empty circles, 80% proportion of protection, empty diamonds, 40% test and slaughter; prevalences and cumulative incidences are given as straight proportions).

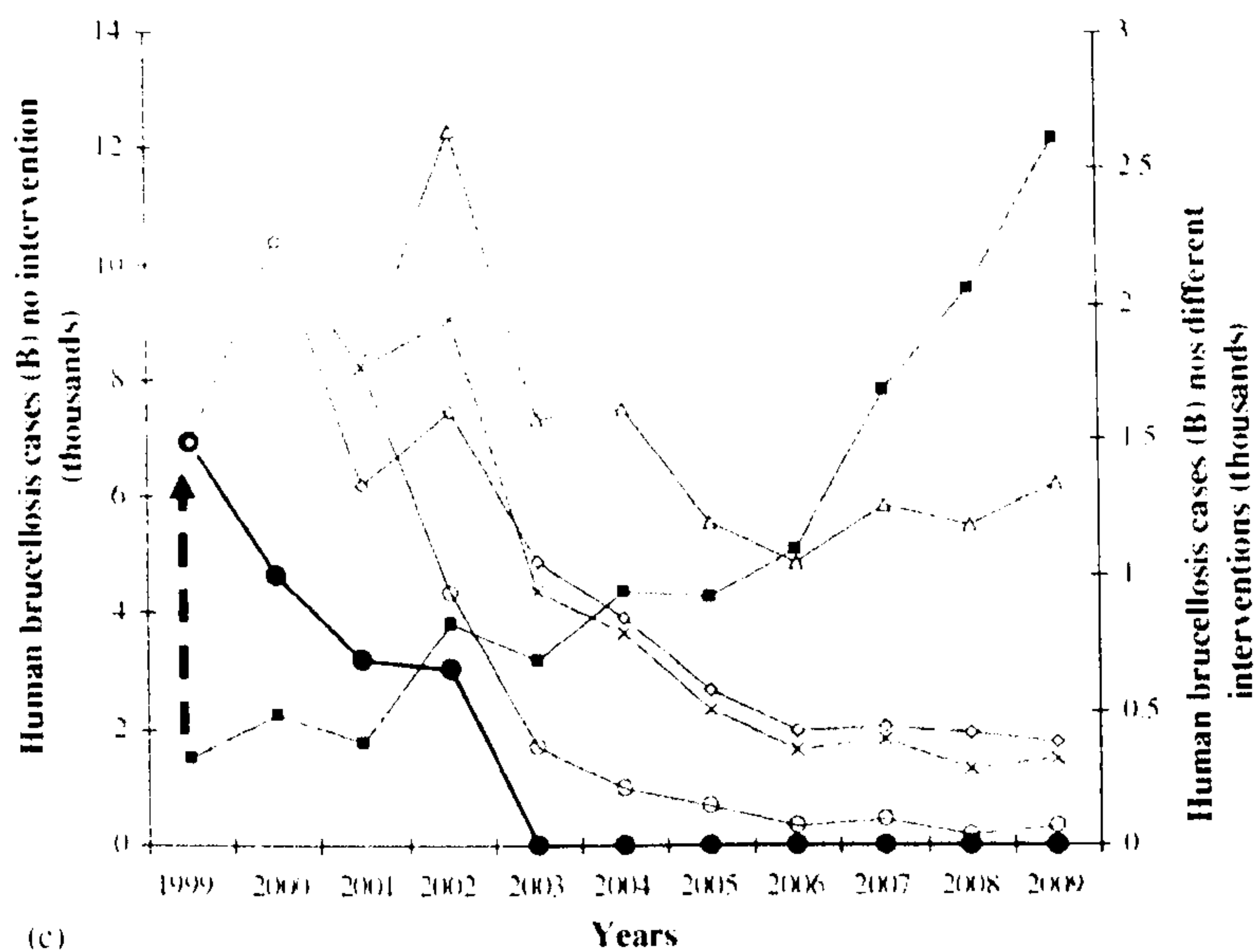


Fig. 6. (Continued).

The fit to the data seems satisfactory but the model captures only the large trends of the diseased compartments of livestock and humans (and not the smaller modulations). An estimation of the susceptible-sheep population for the missing years was done by linear backward extrapolation in analogy to the almost-linear growth trend of the cattle population (see Fig. 2a). A posteriori, the sheep-brucellosis component was refitted to a more complete data set and the contact rate β_s was 3% lower (1.519×10^{-7} against 1.56×10^{-7}) to the previous estimate based on the linear backward extrapolation of the susceptible sheep population. The proportions of infectious sheep and cattle might in fact range in more-narrow bands. Bürki and Sackmann (personal communication) estimate it between 50 and 60%, but the presented range yielded the best fit and is in line with Parnas et al. (1966) who estimated the range of shedders between 22 and 60%. That most human-brucellosis cases found in our model were small ruminant derived is in line with recent isolations of *Brucella* strains from human patients in Mongolia. All isolated strains ($n = 8$) were *B. melitensis* (Nansalma, personal communication).

The estimated threshold coverage of the vaccination must be corrected for the efficacy of the vaccines. The efficacy of Rev1 is considered to be 0.95 (AFSSA) and for S19 to be 0.7 (Nicoletti, 1977; WHO, 1998). This would need a corrected coverage of approximately 50% for sheep and 95% for cattle. The considerations on vaccine efficacy are also in line with observations by Denes (1997) in Mongolia. Our model shows higher numbers of vaccinated animals and a lower reduction of seroprevalence in livestock compared to the reported data. Nicoletti (personal communication, 2002) considers that the vaccine efficacy in mass vaccinations is actually much higher than that obtained in vaccine trials, due to the herd effect. This could explain partially the strong reduction of sheep and cattle prevalence obtained by the reported number of vaccinated animals. The long-term predictions have to be considered with caution, especially due to the recent massive demographic changes in the livestock

populations. The population should recover certainly from the consecutive snow-storm disasters; however, a comprehensive assessment of the effective carrying capacity of Mongolian pasture should inform policy on a sustainable regulation of livestock density.

4.2. Interventions

In general, the model mechanism is able to fit and simulate plausibly the different interventions. But, the long time-step causes oscillations and a lag period of the effect on human disease. The model predicts a decrease of seroprevalence in livestock by the vaccination campaign. After 10 years, the intervention strategies should be reviewed to consider that brucellosis might remain only in certain areas. In cattle, a test-and-slaughter policy should be considered at the end of the mass-vaccination campaign, if compensation could be offered for slaughtered animals. The model can produce estimates of the numbers of animals for which compensation is needed. The vaccination campaign seems more effective to reduce prevalence in sheep than in cattle. This work confirms the control strategy already chosen in the 1970s WHO brucellosis-control project, which effectively reduced human brucellosis through livestock mass vaccination (Kolar, 1977) and contributes a quantitative framework of analysis.

4.3. Limitations of the model

We did not consider geographical differences of the disease prevalence, age dependence, nor could we include goats (which might play an important role in the transmission to humans). The model could become smoother by reducing time steps to half-year or quarter-year intervals. This probably also would reduce the overestimation of the vaccinated animals in our model. We should bear in mind that the quality of the demographic and seroprevalence data are unknown, but the overestimation of the vaccinated animals and the provided coverage figures would indicate that the actual animal numbers are smaller than reported. The model could be used to assess other zoonoses and food-borne diseases. Improvements of the model should include spatial effects and might be formulated using Bayesian Markov Chain Monte Carlo methodology (Marshall et al., 2003)

Acknowledgements

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Appendix A

Data set to which the model was fitted in VensimTM without vaccination intervention (years = 1991–1999) and to which the effect of the vaccination was fitted (years = 1999–2002).

Year	Sheep			Cattle			Humans		
	Number susceptible (<i>U</i>)	Number seropositive (<i>V</i>)	Seroprevalence (%)	Number susceptible (<i>X</i>)	Number seropositive (<i>Y</i>)	Seroprevalence (%)	Number susceptible (<i>A</i>)	Number of annually reported cases (<i>B</i>)	
1991	11,468,330	57,630	0.50	2,765,217	22,044	0.80	2,179,560	108	
1992	11,937,672	72,058	0.60	2,897,395	25,078	0.87	2,212,870	1,192	
1993	12,393,552	99,948	0.81	2,968,915	90,140	3.04	2,246,180	616	
1994	12,873,452	103,818	0.81	3,147,373	61,746	1.96	2,279,490	814	
1995	13,595,133	123,467	0.91	3,276,856	40,242	1.23	2,312,800	937	
1996	13,411,433	149,167	1.11	3,422,561	53,338	1.56	2,347,100	1,158	
1997	14,105,744	113,756	0.81	3,571,865	41,033	1.15	2,379,600	1,122	
1998	15,344,730	108,170	0.70	3,715,283	36,416	0.98	2,413,000	1,308	
1999	15,069,770	121,530	0.81	3,776,780	48,018	1.27	2,446,400	1,482	
2000 ^a	13,876,400	124,888	0.90	3,097,600	46,464	1.50	2,407,500	992	
2001 ^a	11,937,300	23,875	0.20	2,069,600	20,696	1.00	2,442,500	685	
2002 ^a	10,636,602	42,546	0.40	1,884,279	15,074	0.80	2,432,229	652	

Sample sizes for the prevalence estimates ranged between 80,000 and 260,000 in cattle and 100,000 and 340,000 in sheep.

^a For these 3 years, the number of susceptible sheep (*U*) and cattle (*X*) include vaccinated sheep (*W*) and cattle (*Z*), respectively.

Appendix B. Differential equations for the fitting and simulation of vaccination

$$\begin{aligned} \frac{dU}{dt} = & \varepsilon_s V + \tau_{\text{Rev1}} W + \left(\alpha_s (U + V + W) \left(1 - \left(\eta \left(\frac{V}{(U + V + W)} \right) \right) \right) \right) \\ & \times (1 - (c_{ys} \nu_{\text{Rev1}})) - \mu_s U - \delta_s U - \gamma_s \beta_s UV - c_{as} \nu_{\text{Rev1}} \frac{U}{3} \end{aligned} \quad (\text{A.1})$$

$$\frac{dV}{dt} = \gamma_s \beta_s UV - \varepsilon_s V - \mu_s V - \delta_s V - \varphi_s V \quad (\text{A.2})$$

$$\begin{aligned} \frac{dW}{dt} = & c_{as} \nu_{\text{Rev1}} \frac{U}{3} + \left(\alpha_s (U + V + W) \left(1 - \left(\eta \left(\frac{V}{(U + V + W)} \right) \right) \right) \right) \\ & \times (c_{ys} \nu_{\text{Rev1}}) - \mu W - \delta_s W - \tau_{\text{Rev1}} W \end{aligned} \quad (\text{A.3})$$

$$\begin{aligned} \frac{dX}{dt} = & \varepsilon_c Y + \tau_{\text{S19}} Z + \left(\alpha_c (X + Y + Z) \left(1 - \left(\eta \left(\frac{Y}{(X + Y + Z)} \right) \right) \right) \right) \\ & \times (1 - (c_{yc} \nu_{\text{S19}})) - \mu_c X - \delta_c X - \gamma_c \beta_c XY - c_{ac} \nu_{\text{S19}} \frac{X}{3} \end{aligned} \quad (\text{A.4})$$

$$\frac{dY}{dt} = \gamma_c \beta_c XY - \varepsilon_c Y - \mu_c Y - \delta_c Y - \varphi_c Y \quad (\text{A.5})$$

$$\begin{aligned} \frac{dZ}{dt} = & c_{ac} \nu_{\text{S19}} \frac{X}{3} + \left(\alpha_c (X + Y + Z) \left(1 - \left(\eta \left(\frac{Y}{(X + Y + Z)} \right) \right) \right) \right) (c_{yc} \nu_{\text{S19}}) \\ & - \mu_c Z - \delta_c Z - \tau_{\text{S19}} Z \end{aligned} \quad (\text{A.6})$$

$$\frac{dA}{dt} = \alpha_h (A + B + C) + \lambda C - ((\gamma_s \beta_{sh} AV) + (\gamma_c \beta_{ch} AY)) - \mu_h A \quad (\text{A.7})$$

$$\frac{dB}{dt} = ((\gamma_s \beta_{sh} AV) + (\gamma_c \beta_{ch} AY)) - \mu_h B - \kappa B \quad (\text{A.8})$$

$$\frac{dC}{dt} = \kappa B - \mu_h C - \lambda C \quad (\text{A.9})$$

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Human health benefits from livestock vaccination for brucellosis: case study

Felix Roth,¹ Jakob Zinsstag,¹ Dontor Orkhon,² G. Chimed-Ochir,³ Guy Hutton,¹ Ottorino Cosivi,⁴ Guy Carrin,⁴ & Joachim Otte⁵

Objective To estimate the economic benefit, cost-effectiveness, and distribution of benefit of improving human health in Mongolia through the control of brucellosis by mass vaccination of livestock.

Methods Cost-effectiveness and economic benefit for human society and the agricultural sector of mass vaccination against brucellosis was modelled. The intervention consisted of a planned 10-year livestock mass vaccination campaign using Rev-1 livestock vaccine for small ruminants and S19 livestock vaccine for cattle. Cost-effectiveness, expressed as cost per disability-adjusted life year (DALY) averted, was the primary outcome.

Findings In a scenario of 52% reduction of brucellosis transmission between animals achieved by mass vaccination, a total of 49 027 DALYs could be averted. Estimated intervention costs were US\$ 8.3 million, and the overall benefit was US\$ 26.6 million. This results in a net present value of US\$ 18.3 million and an average benefit–cost ratio for society of 3.2 (2.27–4.37). If the costs of the intervention were shared between the sectors in proportion to the benefit to each, the public health sector would contribute 11%, which gives a cost-effectiveness of US\$ 19.1 per DALY averted (95% confidence interval 5.3–486.8). If private economic gain because of improved human health was included, the health sector should contribute 42% to the intervention costs and the cost-effectiveness would decrease to US\$ 71.4 per DALY averted.

Conclusion If the costs of vaccination of livestock against brucellosis were allocated to all sectors in proportion to the benefits, the intervention might be profitable and cost effective for the agricultural and health sectors.

Keywords Brucellosis/veterinary/prevention and control/transmission; Brucellosis, Bovine/prevention and control/transmission; Cattle/immunology; Sheep/immunology; Mass immunization/economics, Human; Cost of illness; Disability evaluation; Intersectoral cooperation; Cost allocation; Cost-benefit analysis; Mongolia (*source: MeSH, NLM*).

Mots clés Brucellose/médecine vétérinaire/prévention et contrôle/transmission; Brucellose bovine/prévention et contrôle/transmission; Bovin/immunologie; Mouton/immunologie; Immunisation de masse/économie; Humain; Coût maladie; Evaluation incapacité; Coopération intersectorielle; Affectation coûts; Analyse coût-bénéfice; Mongolie (*source: MeSH, INSERM*).

Palabras clave Brucelosis/veterinaria/prevencción y control/transmisión; Brucelosis bovina/prevencción y control/transmisión; Bovinos/inmunología; Ovinos/inmunología; Inmunización masiva/economía; Humano; Costo de la enfermedad; Evaluación de la incapacidad; Cooperación intersectorial; Asignación de costos; Análisis de costo-beneficio; Mongolia (*fuelle: DeCS, BIREME*).

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Voir page 874 le résumé en français. En la página 874 figura un resumen en español.

Introduction

Brucellosis is one of the world's major zoonoses, alongside bovine tuberculosis and rabies (1). Brucella infection is endemic in humans and livestock in Mediterranean countries (2, 3). It is also present in Asia, sub-Saharan Africa, and Latin America (4–6). The importance of brucellosis is not known precisely, but it can have a considerable impact on human and animal health, as well as wide socioeconomic impacts, especially in countries in which rural income relies largely on livestock breeding and dairy products. Human brucellosis is caused by exposure to livestock and livestock products. The most important causative bacteria in decreasing

order are: *Brucella melitensis* (small ruminants), *B. abortus* (cattle), *B. suis* (pigs), and *B. canis* (dogs). Infection can result from direct contact with infected animals and can be transmitted to consumers through raw milk and milk products. Human-to-human transmission of the infection does not occur (7).

In humans, the symptoms of disease are extreme weakness, joint and muscle pain, headache, undulant fever, hepatomegaly, splenomegaly, and night sweats (8). Mortality is reported to be negligible, but the illness can last for several years. In animals, brucellosis mainly affects reproduction and fertility, reduces survival of newborns, and reduces milk yield. Mortality of adult animals is insignificant (9).

¹ Swiss Tropical Institute, Swiss Centre for International Health and Department of Epidemiology and Public Health, Basle, Switzerland. Correspondence should be sent to Dr Zinsstag at this address (email: Jakob.Zinsstag@unibas.ch).

² Ministry of Health and Social Welfare, Olympic Street 2, Ulaanbaatar 11, Mongolia.

³ Infectious Disease Research Centre, Ulaanbaatar, Mongolia.

⁴ World Health Organization, Geneva, Switzerland.

⁵ Food and Agriculture Organization of the United Nations (FAO), Rome, Italy.

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Control strategies available to prevent human infection are pasteurization of milk, livestock vaccination, and elimination of infected animals. In Mongolia, livestock rearing and milk production are important branches of the economy, employing approximately 50% of the population. In the 1970s, mass vaccination of livestock successfully reduced the annual incidence in humans to less than one case per 10 000 (J Kolar, personal communication, 1999, J Kolar, personal communication, 2000). After democratic reform, and the shift away from dependence on the former Soviet Union in 1990, human brucellosis re-emerged as a major, but preventable, source of illness. A large survey conducted during 1990–95 among herdsmen and other people who work with animals showed that 16% of the examined population were infected (10). Transmission mainly seems to be an occupational hazard. In contrast, in Saudi Arabia, where consumption of raw milk is important, 30% of the people reported as having brucellosis were aged <15 years (8).

The Mongolian authorities suspect that the high incidence of brucellosis causes significant economic losses. On the basis of recommendations made to WHO (11), a whole-herd vaccination strategy covering 10 years was developed to start in 2000 (12). Very little is known about the economic implications of brucellosis and brucellosis control for human health in any country (13). The particular zoonotic nature of brucellosis needs a multisectoral assessment, including human health, the socioeconomic situation of the concerned population groups, and livestock production.

The main objective of this study was to estimate the cost-effectiveness to human health and the potential net economic benefits of a nationwide mass vaccination programme for livestock over a period of 10 years. In order to present cost-effectiveness and cost-benefit ratios from different perspectives (health sector, agricultural sector, households, and society), a tool was developed that attributed costs and benefits to these different perspectives.

Material and methods

Selection of alternatives

From 1990, Mongolia has practised low-level surveillance, with occasional testing of livestock herds, followed by voluntary slaughter of infected animals. No state compensation is given for slaughtered animals.

Our analysis of the potential benefit of livestock vaccination is based on the vaccination scheme proposed in the Mongolian budget in 2000 for whole-herd vaccination (Appendix A, web version only, available at: <http://www.who.int/bulletin>) within the first six years, this scheme aims to vaccinate all adult animals twice (one-third of the total adult population per year). All animals born during the 10 years of the plan will be vaccinated once (at age <1 year). For the selection of vaccination scenarios, we assumed the reported efficacy for reduction of transmission as the prevented fraction ($1 - R$), where R is the relative risk of disease in those who receive the intervention compared to those who do not (14), and that the vaccines to be used in cattle (strain B19, *Brucella abortus*) and small ruminants (Rev-1, *B. melitensis*) should reduce transmission by at least 65% (15). In addition, a hypothetical efficacy of vaccine of 100% was also tested. Vaccine coverages were assumed to be 50% and 80%, respectively, to allow for frequent problems with cold chains.

These assumptions produced three alternative vaccination scenarios, with percentages for protection from transmission of 32% (65% efficacy \times 50% coverage), 52% (65% efficacy \times 80%

coverage), and 80% (100% efficacy \times 80% coverage). We assumed that different vaccination coverages would not affect the budget for the intervention because the costs of personnel, transport, and vaccine costs would remain very much the same irrespective of whether the farmers and their animals were present or absent when the mobile teams visited.

Form of evaluation

We performed an incremental cost-effectiveness analysis to compare the cost and health effects of the vaccination programme for the human population with the cost and health effects of current practice. The burden of brucellosis on the human population was estimated for different age groups and sexes from data on morbidity and mortality and on the duration of the disease (case-fatality and remission rates). The benefit-cost analysis focused on the net monetary gain associated with different vaccination strategies (current practice vs 32%, 52%, and 80% protection from transmission) for brucellosis prevention and control. The net present value is used as a key evaluation criterion.

Data collection

We developed a conceptual framework to consider human health and livelihood, and animal production and health perspectives. Baseline disease data on reported cumulative incidence of human brucellosis listed by Aimag province for 1990–99 were provided by the Infectious Disease Research Institute in Ulaanbaatar, Mongolia. The Ministry of Agriculture Survey provided data on prevalence of animal brucellosis at the provincial level for cattle, sheep, and goats for 1990–99. The quality of data could not be checked, but ongoing studies on brucellosis in livestock indicate that reported prevalence is underestimated. Our analysis thus is rather conservative.

A household survey was undertaken of 240 patients clinically diagnosed with brucellosis who attended public health facilities between May and August 2000. To complete and compare the data, a Delphi study was organized with two panels: one consisted of 17 specialists in human brucellosis, the other of 16 national experts on animal brucellosis.

Benefit measurement and valuation

Disability-adjusted life year (DALY) is used as a measure of health outcome. An estimate of the burden of disease for brucellosis is not readily available (16), so we therefore estimated the DALYs lost as a result of the disease by assuming that brucellosis is associated with a class II (0.2) disability weight, as the disease is perceived as very painful and affects occupational ability even during periods of remission (17, 18). Average age at onset was calculated for every age group. For the duration of illness, we considered data by Beklemischew on the duration of clinical cure of 1000 patients with brucellosis in the Russian Federation (19). The frequency distribution of clinical disease duration fits best with an exponential function for an average duration of 4.5 years. For duration of disease, we used @Risk expon function, with $\beta = 4.5$ years. For cost effectiveness, we used the median of the cumulated discounted DALYs, which corresponds to a median duration of brucellosis of 3.11 years.

The economic evaluation included the impact on human health costs and income loss, coping costs, and impact on livestock production. Benefits in monetary terms were computed for three different sectors. For the agricultural sector, we considered the benefit of avoidance of losses in animals and animal products; for the public health sector, we considered the benefit

of avoiding costs and for private households with patients suffering from brucellosis, we considered the benefit resulting from avoidance of out-of-pocket payments for treatment, loss of income (opportunity costs), and costs of coping.

The sum of all three mentioned benefits was considered a benefit for society as a whole and represents a monetary valuation of the health benefit. The method avoided double counting of common costs between the public health sector and payments for treatments made by patients. For every sector, the net present value and benefit–cost ratio were computed. The Mongolian Ministry of Agriculture, which started implementation of the vaccination campaign in 2000, established a budget calculation for the whole 10-year campaign of about 11 334 million Mongolian Tugrik (MNT) (equivalent to about US\$ 10.5 million on the basis of an exchange rate of MNT 1080 = US\$ 1 in October 2000) (Appendix A).

Costing

A societal perspective was used to conduct the costing part of the analysis (20). The costing is based on the budget of the Mongolian Ministry of Agriculture for the 10-year vaccination campaign against brucellosis (Appendix A). This budget considers the number of animals to be vaccinated; cost of vaccines (*B. melitensis* Rev-1 and *B. abortus* S19); service costs of vaccination (transportation, cold chain, and veterinary fees); costs related to ear tagging; service costs for surveillance and diagnostic tests; and costs of health education, training, and advocacy for herders. The overhead costs of national and local government authorities that administered the programme were not considered in the calculations, as the marginal cost for adding this brucellosis control programme were expected to be negligible. As all breeders' activities are shared within the family, marginal product lost because of their involvement in the campaign was very low to zero: we assumed that the time a farmer spent on the campaign did not make him lose money from an activity he could have pursued instead. Consequently, the opportunity cost of breeders' time was given a value of zero (21).

Quantities and unit costs for animals and animal products were obtained from the household survey, Delphi panels, and business publications (22). Livestock production was calculated from herd structures and productivity parameters with the *Livestock development planning system* (LDPS2) (23, 24). Quantities and unit costs for the human health sector and opportunity costs of human brucellosis infection were generated by the Delphi panel, patient-based household survey, and Mongolian Ministry of Health. All model calculations were in MNT, with prices from the year 2000 (MNT 1080 = US\$ 1).

Sharing costs among sectors

As the vaccination campaign improves human health through interventions in the veterinary sector, the allocation of costs of the intervention among different sectors had to be decided. Although the benefit side can be assigned easily to the breeders (benefits from livestock production), patients (reduced out-of-pocket expense and coping costs), and public health sector (avoidance of hospitalization and drugs), the costs cannot be assigned wholly to the agricultural sector or to the health sector.

In order to attribute the cost to the different sectors, we applied basic elements of the technique for joint cost allocation in multipurpose projects, known as the "separable costs–remaining benefits" method (25). In the vaccination campaign against bru-

cellosis, all expenditure was associated with animal health, while human health benefit was produced without separable costs. We therefore used an adaptation of the method, in which we regarded all costs as joint costs and allocated the costs proportionally to the benefit. Out of this allocation, the cost-effectiveness of the intervention for human health could be derived, as could measures for economic benefit.

Modelling

To assess the reduction of the effects of brucellosis in humans and animals by its control through vaccination in livestock, we modified and extended the susceptible–infected–recovered models of brucellosis transmission used by Gonzalez-Guzman & Naulin (26) to include animal-to-human transmission (Fig. 1). Poisson regression analyses of existing data on the provincial level showed a significant ecological relation between seroprevalence of brucellosis in cattle and sheep and cumulative incidence of reported human cases. The coefficients from such analyses were used as initial parameter estimates for the fitting of deterministic equations (Vensim; Ventana Systems Inc., Harvard, Massachusetts, USA). The model was validated with human and livestock demographic and disease data from 1991 to 1999 (before the start of the vaccination campaign by steps of one year). The validation of the vaccination intervention used data from the first three years of the ongoing brucellosis mass vaccination campaign in Mongolia (2000–02). The detailed model will be published elsewhere.

Fig. 1 shows the model framework, which is composed of compartments for susceptible sheep and cattle (serologically negative by the Rose Bengal test). We omitted transmission from goats because of the lack of data, but the productivity of goats was considered in the economic analysis by using disease data from sheep. Susceptible sheep and cattle become infected and move to the compartments of seropositive sheep and cattle (Rose Bengal test). We did not consider a compartment of "recovered", because data on seroprevalence were available for validation of the model only. The compartment of seropositive animals is composed of an unknown proportion of infected animals capable of infecting other animals and humans. The transmission (infected sheep and cattle in Fig. 1) is shown in the example of cattle in equation (1), in which γ is the proportion of infectious animals, expressed as a uniform probability distribution, β is the contact rate, X are susceptible cattle, and Y are seropositive cattle.

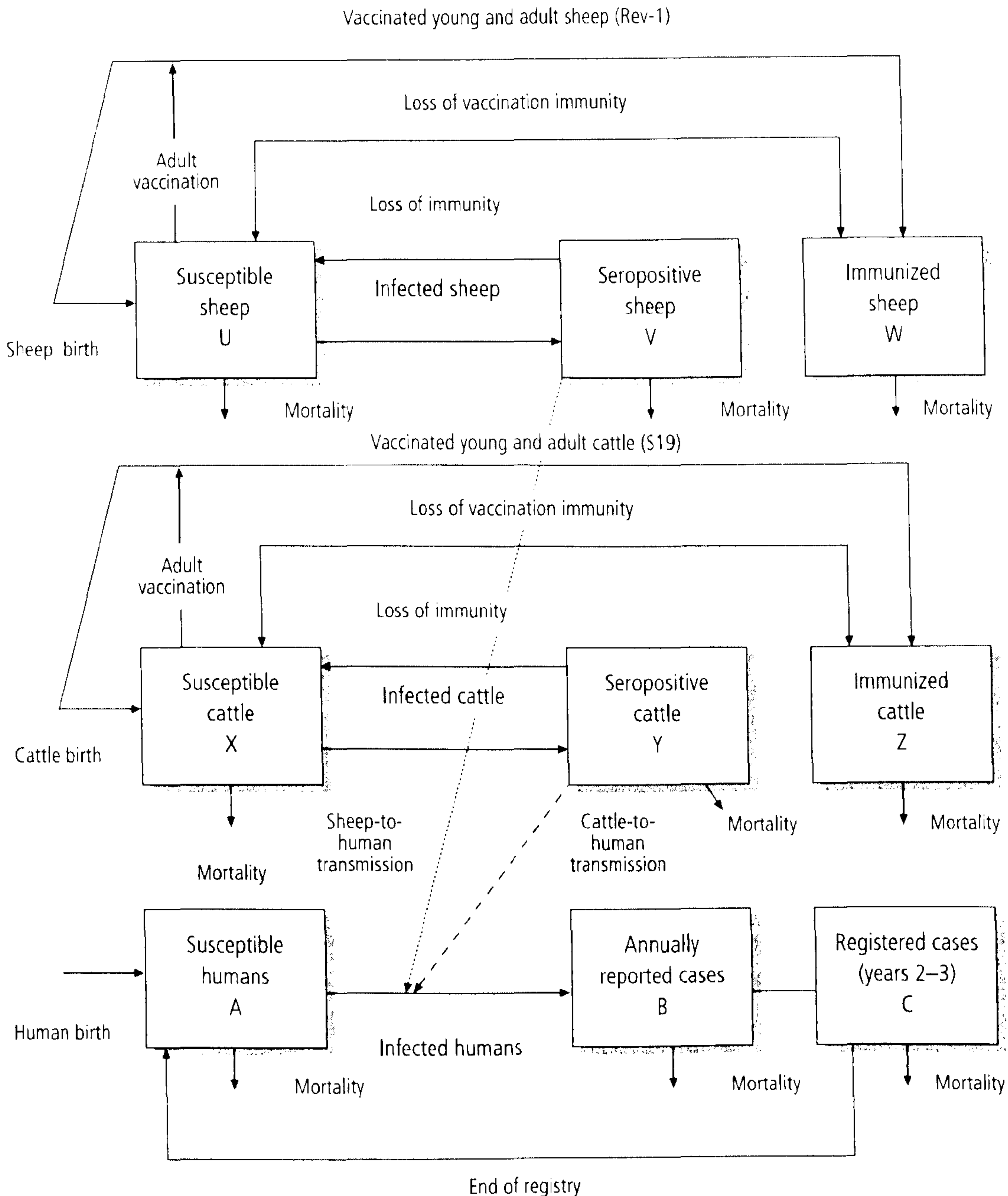
$$\gamma\beta XY \quad (1)$$

Seropositive animals may convert to seronegative animals (loss of immunity). For the fitting of between-animal transmission, the boundaries of the proportion of infective animals were varied to identify the best fit. Transmission to humans is expressed as the additive contributions of transmission from sheep and cattle to humans (sheep-to-human transmission and cattle-to-human transmission in Fig. 1) in equation (2), in which A is the susceptible human population.

$$(\gamma_{cattle} \beta_{cattle} XA) + (\gamma_{sheep} \beta_{sheep} UA) \quad (2)$$

Compartment A represents the whole Mongolian population, as precise estimates of the population at risk are not available. Compartment B represents the annual number of patients newly registered as having brucellosis. The economic analysis was based

Fig. 1. Model for joint human–animal brucellosis transmission in Mongolia (for an explanation of symbols, see text)



on this compartment and accounted for the whole treatment cost, including treatment of chronic cases in the same year. The annual rate of outflow (registry in Fig. 1) of compartment B = 1 by definition. Compartment C represents the patients registered as having brucellosis between year 2 and 3 of state registration (end of registry = 0.5 by definition), after which they are no longer considered as registered brucellosis patients. The model takes Mongolian health policy into account, as it is important to adapt assessments to local health policy decision pathways (27). The estimation of DALYs is also made on compartment B, but by using the duration of untreated brucellosis. The different vaccination scenarios were expressed as the proportions (32%, 52%, and 80%) of vaccinated young and adult sheep and cattle protected from transmission.

Estimates of the transmission parameters obtained by fitting this model were used to simulate various scenarios for 10 years with and without interventions (Appendix B, web version only, available at: <http://www.who.int/bulletin>). Outcomes of the simulations were prevalence in animals and annual cumulative incidence in humans. As inputs into the economic assessment, these were expressed as normal probability functions, with means and standard deviations provided from Monte Carlo sensitivity analysis on the fitted parameters in Vensim, and were linked to human health and livestock productivity (Appendix C, web version only, available at: <http://www.who.int/bulletin>). Links to prevalence of animal disease were expressed as probability distributions for the decrease in fertility (annual calving or kidding rates) and milk production (Appendix C, ref. 13).

Human health parameters, such as duration of treatment and hospital and outpatient treatment, were derived from the household survey. Human age and sex distributions were obtained from the cases reported in 1999 (Appendix D, web version only, available at <http://www.who.int/bulletin>).

Human health parameters and livestock productivity parameters linked to outcomes of the transmission model and human and livestock demographic population structures (28) were then introduced into a new human and animal health economic model (ECOZOO) developed for this study (Appendices D–G, web version only, available at: <http://www.who.int/bulletin>) (29). ECOZOO is composed of a spreadsheet backbone in Microsoft Excel, which is linked to @Risk stochastic simulation capability and LDPS2. ECOZOO simultaneously computes human and animal effectiveness and economic assessments of health interventions.

Adjustment for timing of costs and benefit

Our economic evaluation was based on the 10-year period of the vaccination programme planned for 2000–09 (base year 1999) by the Mongolian authorities. Limitation of the period of analysis was arbitrary and biased the estimated net benefit of the vaccination campaign downwards. The transmission model therefore was also run for 30 years to estimate time to eradication of the disease, on the assumption that vaccination of young animals would continue in the same way. For consistency reasons, the monetary benefits, costs, and health benefits were discounted at the same rate. A discount rate of 5% was used (30), with a rate of 3% used in the sensitivity analysis.

Allowance for uncertainty

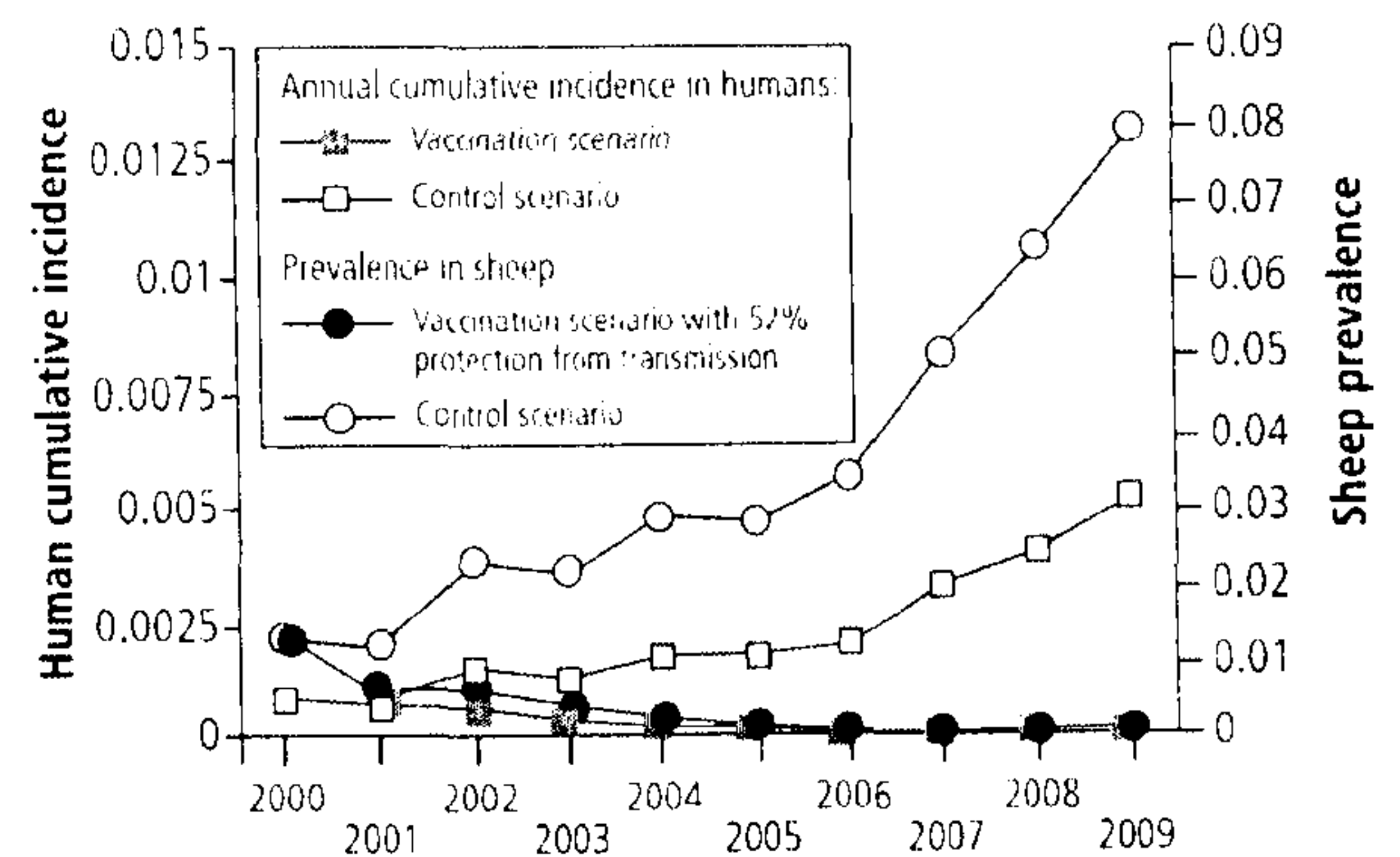
The uncertainty of disease frequency outputs of the deterministic models, health care unit costs, health care units, livestock numbers, livestock product prices, and livestock production parameters was expressed as probability distribution functions using @Risk. Distributions of the societal benefit–cost ratios were then calculated for the different sectors with a latin hypercube sampling type, with 500 iterations on 180 different variables specified as @Risk functions. The relative contribution of the different variables was explored in an automatic sensitivity analysis in @Risk. Sensitivities were expressed as dimensionless, normalized regression coefficients (R-square). Manual sensitivity analyses were done at the level of the economic model by varying selected input parameters (scenarios of 32%, 52%, and 80% protection and 3% and 5% discount rates).

Results

Incremental analysis to compare relevant alternatives

The protection achieved depends on the efficacy of the available vaccines and the vaccine coverage. We assumed that different vaccination coverages do not affect the budget for the intervention for comparisons of annual cumulative incidence of brucellosis in humans between different protection scenarios. When the scenario of 32% protection from transmission was considered, the incidence dropped from six cases per 10 000 at the beginning of the programme to five cases at the end of the programme, whereas with the scenario of 52% protection from transmission it dropped to one case per 10 000 with the same costs involved (Fig. 2). The scenario of 52% protection considered the observed efficacy of S19 (15) and Rev-1 vaccines and a feasible level of coverage (Mikolon A, personal communication, 2000).

Fig. 2. Effect of livestock brucellosis vaccination on humans. Prevalence and cumulative incidences are given as straight proportions



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Major outcomes

Table 1 presents the major economic outcomes by scenario. When the scenario of 52% protection and 5% discount rate was considered, an average number of 61 070 (median 49 027) DALYs could be averted through use of the intervention. The same scenario showed discounted intervention costs of MNT 8957 million (about US\$ 8.3 million) and an overall discounted benefit of MNT 28 753 million (about US\$ 26.6 million). This results in a net profit value of MNT 19 796 million (about US\$ 18.3 million) and a benefit–cost ratio for society of 3.2 (range 2.27–4.37).

Cost-sharing scenario

We developed a cost-sharing scenario to take into consideration the multisectoral effects of the intervention (Table 2). This derived a realistic ratio for cost-effectiveness and profitability of the intervention. If costs of the intervention were shared in proportion to the benefit of each sector, the public health sector would contribute 11% to the intervention costs, giving a cost-effectiveness of US\$ 19.1 (95% confidence interval 5.3–486.8) per DALY averted (Table 3). If private economic gain because of improved human health was included, the health sector would contribute 42% to the intervention costs and the cost-effectiveness would decrease to US\$ 71.4 (19.7–1824.1) per DALY averted.

Sensitivity analysis of benefit–cost ratio and DALYs

A sensitivity analysis of the benefit–cost ratio was done by Monte Carlo simulation in @Risk, with 180 variables expressed as probability distributions (31). The most sensitive parameters were hospital cost (sensitivity 0.69), transport cost (0.36), meat price (0.25), human cumulative incidence (0.2), cashmere price (0.19), unit doctor's fee (0.14), and unit cost of hospital food (0.13). All other variables had sensitivities <0.1. The DALY estimate was highly sensitive to the duration of disease (sensitivity = 0.96) and disease incidence (0.15).

Discussion

At present, the health sector has to bear the cost of human brucellosis at a level of nearly 60 cases per 100 000 per year because of the lack of an effective control programme in the livestock sector. As human brucellosis originates essentially from livestock and livestock products, the health sector is expected to

profit if brucellosis in livestock is controlled. Although it would not be cost effective for the health sector to cover the full cost of the programme, it could be asked to contribute a share (such as the share suggested by our cost allocation model) that would make the programme cost effective from the health sector perspective.

Table 2 shows that with the cost-sharing scenario, the intervention could be profitable for the health and agricultural sectors. The Ministry of Agriculture could meet its share of the project costs, possibly with donor support. As livestock breeders are likely to be the most favoured beneficiaries of the vaccination campaign (economically), they might be willing to contribute to the campaign, and clearly there is some interest from the public sector in attaining a higher degree of cost recovery from this group.

The patients are the second group of beneficiaries. As patients would have contracted brucellosis if there had been no intervention, they avoid out-of-pocket expenses and income loss. As there is no way of identifying people who might have avoided infection, no mechanism would allow their contribution to the intervention costs to be obtained. As shown in Table 2, however, the campaign would still be profitable to the public health sector, if less than 85.6% (3240/3782) of the costs are attributed to this sector. The case for attribution of private costs that result from disease to the public health sector can be strengthened through the argument of poverty reduction. When a patient is ill from brucellosis, this has a strong impact on the household

economy in terms of out-of-pocket contributions to health costs and change in income. Brucellosis mass vaccination for livestock may thus contribute towards alleviating poverty in households.

Health expenditure for Mongolia in 1998 amounted to US\$ 33.2 million, and international donor support to the Mongolian health sector was US\$ 4 million (12%) (32). Given this background, the intervention costs for the vaccination programme (US\$ 10.5 million over 10 years) are very significant. With the cost-sharing scenario, the multisectoral character of interventions to control zoonotic diseases is taken into consideration. When we computed the cost-effectiveness ratio from the Ministry of Health's point of view, US\$ 19.1 per DALY would be averted, which falls into WHO's range of highly cost-effective programmes (<US\$ 25 per DALY averted) (33). When we included the incremental costs of patients in the total incremental costs, US\$ 71.4 per DALY would be averted, which is still in the next band of cost effective (<US\$ 150 per DALY averted). In our context, the cost-effectiveness result of US\$ 19.1–71.4 (costs allocated to patients plus public health sector costs) per avoided DALY represents 5.7–21.5% of the gross domestic product per capita (US\$ 333 in 1999 (34)) and therefore also can be rated as attractive from this point of view.

Our assessment is based on a disability weight of 0.2. More research is needed to establish the disability weight of human brucellosis. The median duration of disease (3.11 years) we used (on the basis of on data from Beklemischew (20)) tallies

Table 1. Summary results of a 10-year brucellosis vaccination campaign in Mongolia

Variable	Protection					
	80%		52%		32%	
	Discounted rate		Discounted rate		Discounted rate	
	3%	5%	3%	5%	3%	5%
Scenario						
Vaccine efficacy (%)	100		65		65	
Vaccine coverage (%)	80		80		50	
Protected animals (%)	80		52		32.5	
Health benefits						
Discounted cumulated median DALYs ^a						
Disability class weight I	Not done	Not done	Not done	24 530	Not done	Not done
Disability class weight II	63 217	52 618	58 675	49 027	52 618	42 394
Intervention costs (MNT million) ^{b,c}	9 806.2	8 957.3	9 806.2	8 957.3	9 806.2	8 957.3
Benefits in monetary terms (MNT million)						
A Agriculture sector ^d	21 702.5	18 850.0	19 133.8	16 611.6	13 630.5	11 816.8
B Public health system ^e	4 062.7	3 513.1	3 760.9	3 240.3	3 237.7	2 779.9
C Out of pocket contributed for health care ^f	6 718.6	5 809.8	6 219.6	5 358.7	5 354.3	4 597.3
D Private income ^g	4 441.8	3 841.0	4 111.9	3 542.8	3 539.8	3 039.4
B+C ^h	10 781.3	9 322.9	22 894.7	8 599.0	8 592.0	7 377.2
A+C+D ⁱ	32 862.9	28 500.8	29 465.3	25 513.1	22 524.6	19 463.5
A+B+C+D ^j	36 925.6	32 013.9	33 226.2	28 753.4	25 762.3	22 233.4

^a DALY = disability-adjusted life year.
^b Budget of Ministry of Agriculture.
^c MNT = Mongolian Tugrik.
^d Discounted net incremental profit to the breeder.
^e Discounted reduction of costs in public health sector.
^f Discounted reduction of health costs to patient.
^g Discounted reduction of income loss to patient.
^h Discounted total benefit to overall health sector.
ⁱ Discounted total benefit to private society.
^j Discounted total benefit to society.

Table 2. Scenario for allocation of intervention cost and benefit over the sectors with 52% animals protected and 5% discount rate

Sector	Allocation of intervention (million MNT) ^a		Net present value ^b (million MNT)	Benefit–cost ratio ^c
	Costs	Benefits		
Agriculture				
Breeders	5 174.9	16 611.6	11 436.7	3.2
Public	0	0	0	
Total	5 174.9	16 611.6	11 436.7	3.2
Human health				
Public health				
Ministry of Health, central government	1 009.4	3 240.3	2 230.9	3.2
Health insurance scheme, health insurance fund	0	0	0	
Patients				
Out of pocket contribution to health costs	1 669.3	5 358.7	3 689.4	3.2
Change in household income	1 103.7	3 542.8	2 439.1	3.2
Total	3 782.4	12 141.8	8 359.4	3.2
Total private sector	7 947.9	25 513.1	17 565.2	3.2
Total society	8 957.3	28 753.4	19 796.1	3.2

^a US\$ 1 = MNT 1080 (October 2000).^b Benefits minus costs.^c Benefits over costs (range 2.27–4.37).

Table 3. Cost effectiveness for human health in scenario with 52% animals protected and 5% discount rate

Discounted intervention cost per DALY saved	Median ^a	
	Disability class II	Disability class I
Public health sector perspective		
MNT	20 589 (5676–525 729)	41 150 (10 925–1 157 569)
US\$ ^b	19.1 (5.3–486.8)	38.1 (10.1–1071.8)
% of gross domestic product/capita ^c	5.7 (1.6–146.2)	11.4 (3–321.9)
Societal perspective ^d		
MNT	77 149 (21267–1 970 000)	154 195 (40 938–4 337 615)
US\$	71.4 (19.7–1824.1)	142.8 (37.9–4016.3)
% of gross domestic product /capita	21.5 (5.9–547.9)	42.9 (11.4–1206.3)

^a Lower confidence limit 2.5% quantile and upper confidence limit 97.5% quantile.^b US\$ 1 = 1080 MNT (October 2000).^c Gross domestic product/capita = MNT 359 583 (23).^d For public health sector avoided out-of-pocket health costs and change in household income.

with the Mongolian policy to register brucellosis cases over a period of three years. The efficacies of the livestock vaccines in the field are probably higher than the efficacies used (herd effect) (P Nicoletti, personal communication, 2002). This would make the scenario of 80% protection (benefit–cost ratio 3.57) very likely.

Further benefits might well result. Farmers and their families should be informed about risky behaviour during the lambing season and the minimal hygiene requirements. Control of brucellosis could have far-reaching effects for the Mongolian economy by opening up new international trade opportunities for livestock. The true value of agricultural production might be higher than that calculated if higher value markets were opened up as a result of brucellosis control. On the other hand, the market prices in 2000 used in the current analysis may overstate the value of increased production, as increased supply might not be countered by increased demand and thus would lead to

decreased prices. This could, however, lead to consumer welfare effects, as consumers could either purchase more livestock products for the same level of expenditure or consume the same amount of livestock products but spend less of their disposable income. Overstocking, which could result in permanent degradation of the carrying capacity of the land, could lead to a situation in which the incremental agriculture production is less than predicted. It is impossible, however, to predict the future size of herds — for example, recent snow disasters and droughts in 2000 and 2001 caused an estimated loss of 7 million animals (and a loss of US\$ 250 million (35)), and, in the affected areas, restocking is needed. Brucellosis mass vaccination for livestock thus also may contribute to poverty alleviation for breeders.

Conclusion

Mass vaccination of livestock against brucellosis in Mongolia would be cost effective and would result in net economic benefit

if interventions costs were shared between the different beneficiaries on the basis of an intersectoral economic assessment. The presented trans-sectoral analysis is applicable to other zoonoses and environmental threats to public health and contributes to the perception that interventions in the livestock sector can control disease transmission to humans (36). ■

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Conflicts of interest: none declared.

Résumé

Avantages pour l'homme de la vaccination du cheptel contre la brucellose : étude de cas

Objectif Estimer l'intérêt économique et le rapport coût/efficacité – répartition comprise des avantages économiques – des progrès sanitaires obtenus en Mongolie en procédant à la vaccination de masse du cheptel contre la brucellose.

Méthodes Le rapport coût/efficacité et l'intérêt économique de la vaccination de masse contre la brucellose pour la société humaine et le secteur agricole ont été modélisés. L'intervention a consisté à planifier sur 10 ans la vaccination de masse du cheptel par la souche Rev-1 pour les petits ruminants et S19 pour les bovins. Le principal résultat obtenu a été le rapport coût/efficacité, soit le coût par années de vie ajustées sur l'incapacité (DALY) évitées.

Résultats Dans l'hypothèse d'une diminution de 52 % de la transmission de la brucellose chez l'animal grâce à la vaccination, on peut éviter 49 027 DALY. On estime le coût de cette intervention à US \$8,3 millions et le gain brut à US \$26,6 millions. Le bénéfice

net s'établit donc à US \$18,3 millions, avec un rapport moyen coût/avantages pour la société de 3,2 (2,27–4,37). Si l'on répartissait les coûts de cette intervention entre les secteurs en fonction des bénéfices qu'ils en retirent, la santé publique devrait contribuer à hauteur de 11 % et obtiendrait un rapport coût/efficacité de US \$19,1 par DALY évitée (intervalle de confiance 95 % : 5,3–486,8). En revanche, si l'on inclut dans le calcul les bénéfices privés dus à l'amélioration de la santé humaine, le secteur de la santé devrait alors contribuer à hauteur de 42 % des coûts de l'intervention, ce qui ramène le rapport coût/efficacité à US \$74,1 par DALY évitée.

Conclusion Si l'on répartit les coûts de la vaccination du cheptel contre la brucellose en fonction des bénéfices que retire chaque secteur de cette intervention, celle-ci pourrait s'avérer profitable et rentable pour la santé et l'agriculture.

Resumen

Beneficios para la salud humana de la vacunación del ganado contra la brucelosis: estudio de casos

Objetivo Estimar el beneficio económico, la relación costo-eficacia y la distribución de los beneficios para la salud humana reportados por la vacunación masiva del ganado contra la brucelosis en Mongolia.

Métodos Se modelizaron la relación costo-eficacia y el beneficio económico para la sociedad y el sector agrícola de la vacunación masiva contra la brucelosis. La intervención consistió en una campaña de 10 años de vacunación masiva del ganado, basada en la administración de la vacuna Rev-1 para pequeños rumiantes y la vacuna S19 para el ganado bovino. Como variable de

evaluación se utilizó la relación costo-eficacia, expresada como costo por año de vida ajustado en función de la discapacidad (AVAD) evitado.

Resultados En un escenario de reducción del 52% de la transmisión de brucelosis entre los animales, gracias a la vacunación masiva, se pudo evitar un total de 49 027 AVAD. El costo estimado de la intervención ascendió a US\$ 8,3 millones, y el beneficio global a US\$ 26,6 millones. Ello se traduce en un valor neto de US\$ 18,3 millones y una relación beneficio-costo media para la sociedad de 3,2 (2,27–4,37). Si los distintos sectores

compartieran los costos de la intervención en proporción al beneficio de cada uno, el sector de salud pública contribuiría con un 11%, lo que arroja una relación costo-eficacia de US\$ 19,1 por AVAD evitado (intervalo de confianza del 95%: 5,3–486,8). Incluyendo el beneficio económico privado resultante de la mejora de la salud humana, el sector de la salud debería contribuir con

el 42% a los costos de intervención, y la relación costo-eficacia aumentaría a US\$ 71,4 por AVAD evitado.

Conclusión Si los costos de la vacunación del ganado contra la brucelosis se asignaran a todos los sectores proporcionalmente a los beneficios, la intervención podría ser rentable y costoeficaz para los sectores agrícola y sanitario.

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Appendix A. Budget and vaccination scheme of the Mongolian Ministry of Agriculture for a whole-herd vaccination programme of brucellosis in cattle and small ruminants in Mongolia^a (MNT millions^b)

Intervention cost per year	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Testing	87.56									
Vaccination of adult sheep and goats ^c	382.84	266.05	244.14							
Second vaccination of adult sheep and goats ^d				382.84	266.05	244.14				
Vaccination of cows ^c	119.85	72.75	48.60							
Second vaccination of cows ^d				119.85	72.75	48.60				
Vaccination of bulls	7.09	7.09	7.09	7.09	7.09	7.09	7.09	7.09	7.09	7.09
Vaccination of newborn sheep and goats ^e	428.70	428.70	428.70	428.70	428.70	428.70	428.70	428.70	428.70	428.70
Vaccination of newborn calves ^e	129.43	129.43	129.43	129.43	129.43	129.43	129.43	129.43	129.43	129.43
Cost of testing							8.52	6.68	8.41	
Ear tags	325.28	325.28	325.28	325.28	325.28	325.28	325.28	325.28	325.28	325.28
Training		50.00								
Annual intervention costs	1 480.74	1 279.29	1 183.23	1 393.18	1 229.29	1 183.23	899.02	897.17	898.90	890.49
Cumulative intervention costs 10 years										11 334.54
Discounted cumulative annual intervention costs at end of year										
5%	1 410.23	2 570.58	3 592.70	4 738.87	5 702.05	6 585.00	7 223.91	7 831.15	8 410.59	8 957.28
3%	1 437.61	2 643.46	3 726.29	4 964.11	6 024.50	7 015.44	7 746.42	8 454.66	9 143.59	9 806.20

^a Budget assumes stable livestock population and considers number of animals to be vaccinated; cost of vaccines (*B. melitensis* (Rev-1) and *B. abortus* (S19)); service costs of vaccination (transportation, cold chain, and veterinary fees); costs related to ear tagging; service costs for surveillance and diagnostic tests; and costs of health education, training, and advocacy for herders.

^b Reference for cost is year 2000.

^c Adult animals (first vaccination).

^d Adult animals (second vaccination).

^e Young animals (less than one year old).

Appendix B. Compartments, fitted parameters, and differential equations in 1999 to 2009 by one-year steps

Variable	Value
Compartments size in 1999	
Sheep	
Susceptible (U)	15 069 770
Seropositive (V)	121 530
Cattle	
Susceptible (X)	3 776 780
Seropositive (Y)	48 018
Humans	
Susceptible (A)	2446400
Newly reported cases annually (B)	1482
Registered cases between years 2 and 3 of registration (C)	2066
Parameter estimates	
Proportion of infectious seropositive cattle (V) (γ_s)	Random uniform (0.2, 0.7)
Immunity loss constant sheep (ϵ_s)	0
Sheep–human contact rate (β_{sh})	1.12738e-008
Mortality rate of sheep (μ_s)	0.79 ^a
Birth rate of sheep (α_s)	0.83
Sheep contact rate (β_s)	1.56082e-007
Decrease of fertility (η)	Random uniform (0.15, 0.5) (C1)
Proportion of infectious seropositive cattle (Y) (γ_c)	Random uniform (0.1, 0.7)
End of registry constant (λ)	0.5 (Def ^b)
Registry change (κ)	1 (Def)

Appendix B. Compartments, fitted parameters, and differential equations in 1999 to 2009 by one-year steps

Variable	Value
Compartments size in 1999	
Sheep	
Susceptible (U)	15 069 770
Seropositive (V)	121 530
Cattle	
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Seropositive (Y)	48 018
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Proportion of infectious seropositive cattle (V) (γ_s)	Random uniform (0.2, 0.7)
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Sheep–human contact rate (β_{sh})	1.12738e-008
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Birth rate of sheep (α_s)	0.83
Sheep contact rate (β_s)	1.56082e-007
Decrease of fertility (η)	Random uniform (0.15, 0.5) (C1)
Proportion of infectious seropositive cattle (Y) (γ_c)	Random uniform (0.1, 0.7)
End of registry constant (λ)	0.5 (Def ^b)
Registry change (κ)	1 (Def)
Cattle animal contact rate (β_c)	3.49736e-007
Cattle animal human contact rate (β_{ch})	2.11247e-009
Cattle birth rate (α_c)	0.28
Human birth rate (α_h)	0.018159
Human mortality rate (μ_h)	0.00333868
Cattle immunity loss constant (ϵ_c)	0
Cattle mortality rate (μ_c)	0.23 ^c
Vaccine efficacy of Rev 1 (v_{Rev-1})	0.65 ^d
Vaccine efficacy of S19 (v_{S19})	0.65 ^e
Inverse duration vaccination protection S19 (τ_{S19})	Random uniform (0.125, 0.142)
Inverse duration vaccination protection Rev-1 (τ_{Rev-1})	Random uniform (0.2, 0.25)
Vaccination coverage (adult) sheep (c_{as})	
No vaccination	0
Scenario 5065 ^f	0.5
Scenario 8065 ^g	0.8
Scenario 80100 ^h	0.8
Proportion of young sheep vaccinated (c_{ys})	
No vaccination	0
Scenario 5065	0.5
Scenario 8065	0.8
Scenario 80100	0.8
Vaccination coverage (adult) cattle (c_{ac})	
No vaccination	0
Scenario 5065	0.5
Scenario 8065	0.8
Scenario 80100	0.8
Proportion of young cattle vaccinated (c_{yc})	
No vaccination	0
Scenario 5065	0.5
Scenario 8065	0.8
Scenario 80100	0.8

(Appendix B, cont.)

Variable	Value
Differential equations for the fitting and simulation of vaccination	
$\frac{dU}{dt}$	$= \epsilon_i V + \tau_{Rev1} W + (\alpha_i (U + V + W) (1 - (\eta (\frac{V}{(U + V + W)})))) (1 - (c_{yi} v_{Rev1})) - \mu_i U - \gamma_i \beta_i UV - c_{ai} v_{Rev1} (0.333) U$
$\frac{dV}{dt}$	$= \gamma_i \beta_i UV - \epsilon_i V - \mu_i V$
$\frac{dW}{dt}$	$= c_{ai} v_{Rev1} (0.333) U + (\alpha_i (U + V + W) (1 - (\eta (\frac{V}{(U + V + W)})))) (c_{yi} v_{Rev1}) - \mu W - \tau_{Rev1} W$
$\frac{dX}{dt}$	$= \epsilon_c Y + (\alpha_c (X + Y + Z) (1 - (\eta (\frac{Y}{(X + Y + Z)})))) (1 - (c_{yc} v_{S19})) - \mu_c X - \gamma_c \beta_c XY - c_{ac} v_{S19} (0.333) X + \tau_{S19} Z$
$\frac{dY}{dt}$	$= \gamma_c \beta_c XY - \epsilon_c Y - \mu_c X$
$\frac{dZ}{dt}$	$= c_{ac} v_{S19} (0.333) X + (\alpha_c (X + Y + Z) (1 - (\eta (\frac{Y}{(X + Y + Z)})))) (c_{yc} v_{S19}) - \mu_c Z - \tau_{S19} Z$
$\frac{dA}{dt}$	$= \alpha_b (A + B + C) + \lambda C - ((\beta_{cb} \gamma_c AY) + (\beta_{ib} \gamma_i AV)) - \mu_b A$
$\frac{dB}{dt}$	$= ((\beta_{cb} \gamma_c AY) + (\beta_{ib} \gamma_i AV)) - \mu_b B - \kappa B$
$\frac{dC}{dt}$	$= \kappa B - \mu_b C - \lambda C$

- ^a 0.83 during vaccination campaign, accounts for stable sheep population assumption.
- ^b Def = definition.
- ^c 0.28 during vaccination campaign accounts for stable cattle population assumption.
- ^d Also accounts for loss of efficacy in field.
- ^e Also accounts for loss of efficacy in field (C2).
- ^f 5065 = scenario with 50% coverage and 65% efficacy.
- ^g 8065 = scenario with 80% coverage and 65% efficacy.
- ^h 80100 = scenario with 80% coverage and 100% efficacy.

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Appendix C. Key functions used to link disease outcome to human health and livestock productivity

Area	Definition
Human health	
Number of cases	= (Population/proportion of age and sex class) ^a exposure constant ^b
Livestock productivity	
Fertility	= Annual number of offspring per breeding female = Baseline fertility ^c × (1 – (Beta-Pert (10%; 15%; 50%) ^d × prevalence))
Cattle milk production	= Annual milk production per lactating female ^e = Baseline milk production ^e × (1 – (Beta-Pert (10%; 15%; 25%) ^f × prevalence))

^a Cumulative incidence.
^b Age- and sex-specific exposure constant, derived from the proportion of the respective age or sex group among those with disease to their respective proportion in the total population (D1) based on the reported brucellosis cases in 1999 (Appendix B).
^c Baseline proportion of annual number of offspring per breeding female in cattle, sheep, and goats.
^d Beta-Pert Distribution (D2) with minimum, most likely and maximum decrease of fertility among diseased (considers abortions, sterility, and mortality of newborn) (Appendix C) (D3).
^e Baseline annual milk production per breeding female.
^f Reduction of milk production among seropositive adult female animals (Appendix C) (D3).

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C2. *Guide to using @Risk. Advanced risk analysis for spreadsheets*. Newfield (NY): Palisade Corporation Inc; 1997. p. 319.
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Appendix D. Calculation of exposure constants^a

Population	Human population of Mongolia in 1999	Proportion of total population (a)	Reported human brucellosis cases in 1999	Proportion of all brucellosis cases (b)	Exposure constant (e)
Children					
Aged <5 years	193 900	0.08	15	0.01	0.0008
Aged 5–15 years	604 500	0.25	152	0.10	0.0250
Women	834 900	0.34	611	0.41	0.1394
Men	813 100	0.33	704	0.48	0.1584
Total	2 446 400		1482		

^a Exposure constants, $e = a \times b$, calculated based on 1999 population and reported brucellosis data (23, Ministry of Health, personal communication).

Appendix E. List of input variables used as @Risk functions

Name	@Risk function
Disease data from the transmission model ^a	
Prevalence (p)	
In unvaccinated animals (sheep and cattle) for years 1 to 10	Normal (mean, Standard deviation)
In vaccinated animals (sheep and cattle) for years 1 to 10	Normal (mean, Standard deviation)
Cumulative incidence (c)	
In humans if animals unvaccinated for years 1 to 10	Normal (mean, Standard deviation)
In humans if animals vaccinated for years 1 to 10	Normal (mean, Standard deviation)
Livestock prices (MNT) (E1)	
Sheep	
Meat off farm (/kg)	Normal (754;311)
Hides off farm (/hide)	Normal (3617;1322)
Goats	
Cashmere (/kg)	Normal (34583;5485)
Meat off farm (/kg)	Normal (754;311)
Hides off farm (/hide)	Normal (7083;4875)
Cattle	
Meat off farm (/kg)	Normal (692;248)
Hides off farm (/hide)	Normal (14083;2476)
Decrease in livestock production (E2)	
Fertility (sheep, goats, cattle)	(Beta-Pert (10%; 15%, 50%)
Milk production (cattle)	(Beta-Pert (10%; 15%; 25%) ⁵)
Human health cost (MNT)	
Hospital costs per day (for Ministry of Health) (E3)	Normal (8646;5194)
Outpatient visits (E4)	Normal (4;2)
Unit cost (out of pocket)	
Current transport (E4)	Pert (0;3200;80000)
Hospital hotel (E4)	Pert (0;2000;25000)
Hospital food (E4)	Pert (0;3000;85000)
Hospital drug (E4)	Pert (0;1500;65000)
Doctor fee (E4)	Pert (0;500;30000)
Loss of income per case (E4)	Pert (9000;30000;500000)

^a Data used were outputs of Vensim Monte Carlo sensitivity analysis.

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E2. Bernues A, Manrique E, Maza MT. Economic evaluation of bovine brucellosis and tuberculosis eradication programmes in a mountain area of Spain. *Preventive Veterinary Medicine* 1997;30:137-49.

E3. Orkhon D, personal communication, 2000.

E4. Roth F, Zinsstag J. *Economic analysis of the brucellosis control in Mongolia*. Geneva: World Health Organization; 2001. p. 225.

Appendix F. Herd composition and productivity parameters in 1999

Variable	Value	Source or basis of calculation or estimate
Cattle		
Total population	3 824 700	(F1)
Female breeders in base year	1 449 800	(F1)
Male breeders in base year	72 490	Estimate a ratio of 1/20 for breeding male to female
Female replacement in base year	391 446	Female calves ' survival rate
Male replacement in base year	144 980	Estimate ratio of 1/20 for preselection of breeding male to female
Other stock in base year	678 634	Total animals — all other categories (animals for offtake)
Female young in base year	543 675	(F1)
Male young in base year	543 675	(F1)
Annual calving rate	0.75	(F1)
Survival rate of replacement	0.72	(F1)
Sheep		
Total population	15 191 300	(F1)
Female breeders in base year	6 846 500	(F1)
Male breeders in base year	136 930	Estimate ratio of 1/50 for breeding male to female
Female replacement in base year	2 244 625	Female lambs ' survival rate
Male replacement in base year	273 860	1/25 for preselection of breeding male to female
Other stock in base year	6 790	Total animals — all other categories (animals for offtake)
Female young in base year	2 841 298	(F1)
Male young in base year	2 841 298	(F1)
Annual lambing rate	0.83	(F1)
Survival rate of replacement	0.79	(F1)
Goats		
Total population	11 033 900	(F1)
Female breeders in base year	4 835 200	(F1)
Male breeders in base year	96 704	Estimate ratio of 1/50 for breeding male to female
Female replacement in base year	1 585 220	Female lambs ' survival rate
Male replacement in base year	193 408	1/25 for preselection of breeding male to female
Other stock in base year	310 152	Total animals — all other categories (animals for offtake)
Female young in base year	2 006 608	(F1)
Male young in base year	2 006 608	(F1)
Annual lambing rate	0.83	(F1)
Survival rate of replacement	0.79	(F1)

References

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Appendix G. Human health input variables from household survey and Delphi panel

Disease characteristic	Value	Source or basis of calculation or estimate
Proportion of chronic cases	0.66	(G1)
Duration of illness (years)	4.5	Data on duration of clinical cure of 1000 brucellosis patients in Russia (G2). ^a
Proportion of inpatient in chronic cases	0.40	(G1)
Average age at onset (for DALYs) (years)		
Women	37.00	(G3)
Men	37.00	(G3)
Children		
Aged 5–15	10.50	(G3)
Aged <5	3.20	(G3)
Inpatient days		
Women	21.00	(G1)
Men	21.00	(G1)
Children		
Aged 5–15	21.00	(G4)
Aged <5	21.00	(G4)
Proportion of hospitalization	0.50	(G1)
Rate of non-formal treatment	0.45	(G1)
Proportion of cases reporting loss of income	0.42	(G1)
Coping cost per case (MNT)	10.00	As we assume that relatives replace for the routine work of the patients and not extra persons have to be engaged; only a symbolic figure has been considered.
Disability-adjusted live years		
Disability weight (D)	0.20	No reference was found so far. A class 0,2 has been chosen since the disease is perceived as very painful. Sensitivity analysis for 0,1 has been done.
Discount rate (r)	0.05	Discount rate 5% with sensitivity analysis 3% based on the interest rate for savings in USD in Mongolia: 5.4% (November 2000) and real growing rate of the Mongolian economy: 3.3% in the last few years.
Age weighing (C)	0.16	(G5)
Parameter of age weighting (beta)	0.04	(G5)
Duration of disability in years (L) (median)	3.11	Data on duration of clinical cure of 1000 brucellosis patients in the Russian Federation (G2). ^a

^a The frequency distribution of clinical disease duration fits best with an exponential function for an average duration of 4.5 years. For duration of disease, we used @Risk expon function with beta = 4.5 years. For cost effectiveness, we used the median of the cumulated discounted DALYs, which corresponds to a median duration of brucellosis of 3.11 years

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